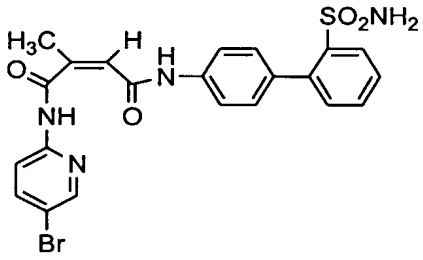
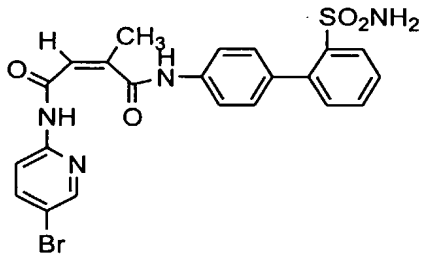
B. Preparation of N-(4-bromophenyl)-N'-(4-[(2-aminosulfonyl)phenyl]phenyl)-maleamic amide.

To a solution of 4-bromoaniline (93 mg, 0.543 mmol) in CH2Cl2 (5 mL) at room temperature, trimethylaluminum (0.82 mL, 2.0 M in hexane, 1.64 mmol) was added dropwise. After the solution was stirred for 30 min at room temperature, compound N-(4-[(2-tert-butylaminosulfonyl)phenyl] phenyl)maleamic methyl ester (113 mg, 0.272 mmol) was added. The mixture was stirred at room temperature for 2 days. The solution was neutralized with 1N HCl to pH 2-3. Water and CH2Cl2 were added, and organic phase was separated, dried over Na2SO4, concentrated in vacuo. The residue was dissolved in TFA (4 mL). It was allowed to stand at room temperature overnight. TFA was removed in vacuo. The residue was purified by HPLC using a gradient of 5% CH3CN in H2O (containing 0.1% TFA) to 95% CH3CN over 60 min. Fractions containing the desired product were pooled, and lyophilized to give a powder (8 mg, yield: 6%). MS 500 and 502 (M + H), 522 and 524 (M + Na). ^{1}H NMR (CD3OD) 8.09 (d, 1H, J = 8 Hz), 7.68 (d, 2H, J = 8 Hz), 7.64 – 7.28 (m, 9H), 6.45 (AB type, 2H).

Examples 44 and 45

Preparation of N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl] phenyl)-2-methylmaleamic amide and N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl]phenyl)-3-methylmaleamic amide.





A. Preparation of N-(5-bromopyridin-2-yl)-methylmaleimide.
A mixture of citraconic anhydride (1.00 mL, 11.1 mmol) and 2-amino-5-bromopyridine (1.93 g, 11.2 mmol) in toluene (60 mL) was heated to reflux overnight.

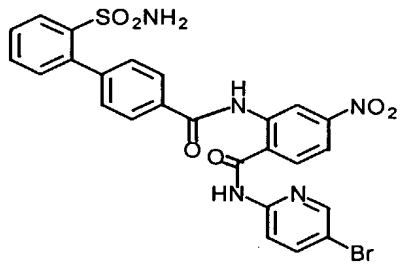
The solution was cooled down, filtered. The filtrate was concentrated in vacuo to give a solid (2.10 g, yield: 71%). MS 267 and 269 (M + H).

B. Preparation of N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl] phenyl)-2-methylmaleamic amide and N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl]phenyl)-3-methylmaleamic amide.

To the solution of 4-(2-aminosulfonylphenyl)aniline (0.170 g, 0.685 mmol) in CH2Cl2 (10 mL) at room temperature, trimethylaluminum (2.0 M in hexane, 2.00 mL, 4.00 mmol) was added dropwise, during which time, white gel-like precipitates came out the solution. It was stirred for 30 min. A solution of N-(5-bromopyridin-2-yl)-methylmaleimide (0.122 g, 0.457 mmol) in CH2Cl2 (5 mL) was added. It was stirred for 1 hour, during which time the precipitates started to dissolve, and the solution became clear. It was stirred for another 2 hours. 1N HCl was added to neutralize the solution to pH 2-3, which resulted in precipitation. The precipitates were collected by filtration, dried on vacuum. The precipitates (75 mg, yield: 32%) were a mixture of 2-methyl and 3-methylmaleamic amide isomers in a ratio of 1 : 5. MS 515 and 517 (M + H), 537 and 539 (M + Na).

Example 46

N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-nitrophenylcarboxamide.



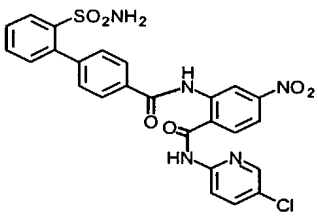
Step 1: A solution of 2-amino-4-nitrobenzoic acid (182 mg, 1 mmol, 1 equiv) in 10 mL of methanol was treated with thionyl chloride in portions until complete reaction. The solvent was evaporated and the residue was dissolved in 10 mL of pyridine. To the solution were added 4-[(2-t-butylaminosulfonyl)phenyl]benzoic acid (330 mg, 1

equiv) and $POCl_3$ (0.93 mL, 10 equiv). The resulting mixture was stirred at rt overnight, quenched by slow addition of water, and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and flash chromatographied to give methyl 2-(4-[(2-t-butylaminosulfonyl)phenyl]phenylcarbonyl)amino-4-nitrobenzoate *(430 mg, 84%)*. MS found for $C_{25}H_{26}N_3O_7S$ $(M+H)^+$: 512.

Step 2: To A solution of 2-amino-5-bromopridine (135 mg, 4.0 equiv) in 5 mL of methylene chloride treated with $AlMe_3$ (2M in hexane, 1 mL, 10 equiv) for 30 min was added methyl 2-(4-[(2-t-butylaminosulfonyl)phenyl]phenylcarbonyl)amino-4-nitrobenzoate (100 mg, 0.2 mmol, 1 equiv). The mixture was stirred at rt overnight, quenched with saturated aqueous potassium sodium tartrate. The organic layer was dried over $MgSO_4$, filtered, evaporated and refluxed in 2 mL of trifluoroacetic acid for 30 min. TFA was then evaporated and HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN gave N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-nitrophenylcarboxamide (42 mg, 36%). MS found for $C_{25}H_{19}BrN_5O_6S$ $(M+H)^+$: 596.

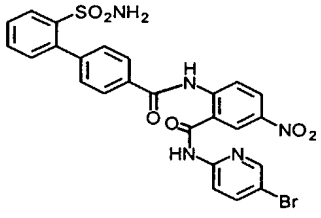
Examples 47-49

The following compounds of Examples 47-49 were prepared according to the procedure described in example 46.



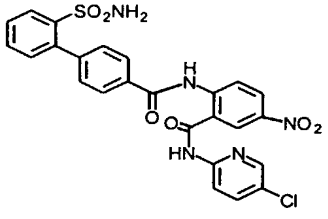
Example 47

MS (M+H): 552



Example 48

MS (M+H): 596

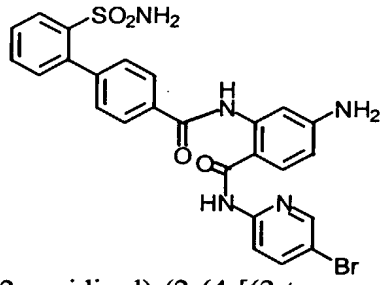


Example 49

MS (M+H): 552

Example 50

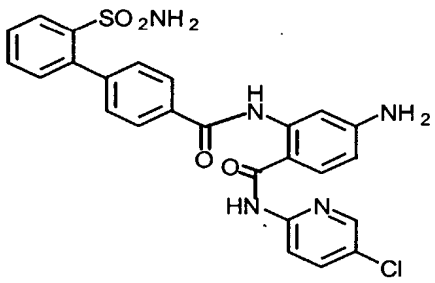
N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide.



A solution of N-(5-bromo-2-pyridinyl)-(2-(4-[(2-t-butylsulfonyl)phenyl]phenylcarbonyl) amino)-4-nitrophenylcarboxamide (65 mg, 0.1 mmol, 1 equiv) in 10 mL of EtOAc was treated with $SnCl_2 2H_2O$ (90 m g, 4 equiv) at reflux for 4 h. The volatile was evaporated and the residue was redissolved in EtOAc, washed with saturated aqueous $NaHCO_3$ and 1N NaOH. The organic layer was dried over $MgSO_4$, filtered and evaporated to give N-(5-bromo-2-pyridinyl)-(2-(4-[(2-t-butylsulfonyl)phenyl]phenylcarbonyl) amino)-4-aminophenyl carboxamide, which was refluxed with 2 mL of TFA for 1h. After removal of TFA by rotavap, the residue was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide (47 mg, 84%). MS found for $C_{25}H_{21}BrN_5O_4S$ $(M+H)^+$: 566.

Example 51

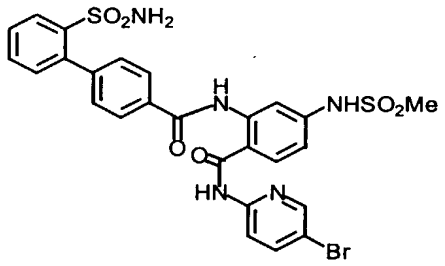
N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide.



This compound was prepared according to the procedure described in example 50. MS found for $C_{25}H_{21}ClN_5O_4S$ $(M+H)^+$: 522.

Example 52

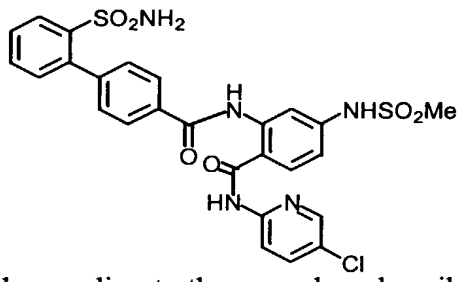
N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide.



A solution of N-(5-bromo-2-pyridinyl)-(2-(4-[(2-t-butylsulfonyl)phenyl]phenylcarbonyl) amino)-4-aminophenyl carboxamide (62 mg, 0.1mmol, 1 equiv) in 3 mL of CH_2Cl_2 was treated with MsCl (23 mg, 2 equiv) and TEA (0.5 mL) at rt for 4 h. The mixture was washed with water and dried over $MgSO_4$, filtered and evaporated. The residue was refluxed with 2 mL of TFA for 1h. After removal of TFA by rotavap, the residue was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide (33 mg, 52%). MS found for $C_{26}H_{23}BrN_5O_6S2$ $(M+H)^+$: 644.

Example 53

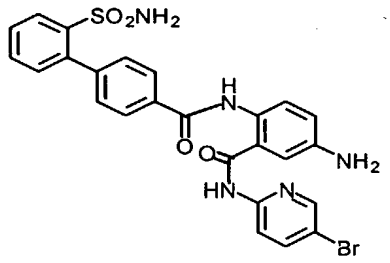
N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide.



This compound was prepared according to the procedure described in example 53. MS found for $C_{26}H_{23}ClN_5O_6S_2$ $(M+H)^+$: 600.

Example 54

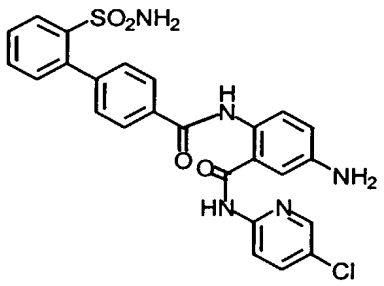
N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide.



This compound was prepared according to the procedure described in example 50. MS found for $C_{25}H_{21}BrN_5O_4S$ $(M+H)^+$: 566.

Example 55

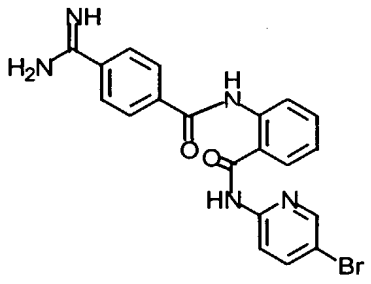
N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide.



This compound was prepared according to the procedure described in example 50. MS found for $C_{25}H_{21}ClN_5O_4S$ $(M+H)^+$: 522.

Example 56

N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)-phenylcarboxamide.

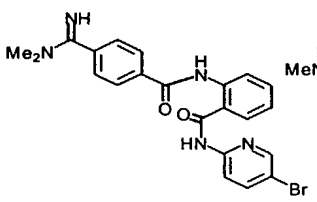


Step 1: A mixture of N-(5-bromo-2-pyridinyl)-(2-amino)phenylcarboxamide (292 mg, 1 mmol, 1.0 equiv), 4-cyano benzoyl chloride (165 mg, 1 equiv), pyridine *(3 mL)* in 10 mL of dichloromethane was stirred at rt overnight, washed with H_2O. The organic layer was dried over $MgSO_4$, filtered, evaporated to give N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)-phenylcarboxamide (349 mg, 70%). MS found for $C_{20}H_{14}BrN_4O_2$ $(M+H)^+$: 421.

Step 2: A stream of HCl(g) was bubbled through a 0°C solution of N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)-phenylcarboxamide (49 mg, 0.1 mmol) in 5 mL of methanol until saturation. The mixture was stirred at rt overnight and evaporated. The resulting residue was treated with ammonium acetate (40 mg) in 10 ml methanol at reflux temperature for 2 h. The solvent was removed at reduced pressure and the crude benzamidine was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)-phenylcarboxamide (31 mg, 70%). MS found for $C_{20}H_{17}BrN_5O_2$ $(M+H)^+$: 438.

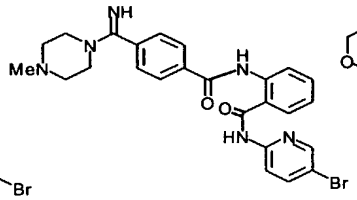
Examples 57-86

The following compounds of Examples 57-86 were prepared according to the procedure described in example 56.



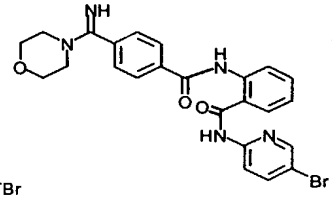
Example 57

MS (M+H): 466



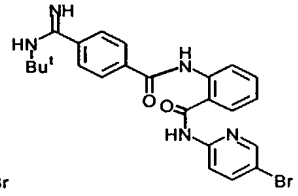
Example 58

MS (M+H): 521



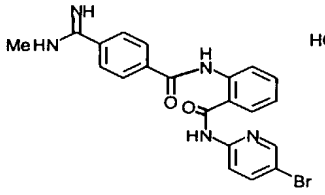
Example 59

MS (M+H): 508



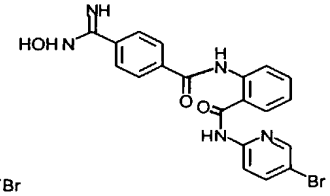
Example 60

MS (M+H): 494



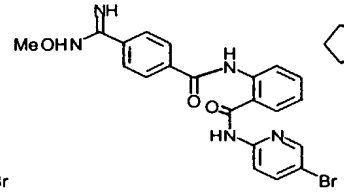
Example 61

MS (M+H): 452



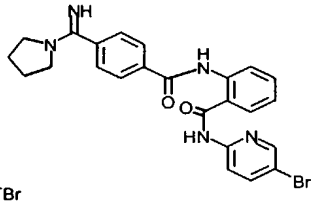
Example 62

MS (M+H): 454



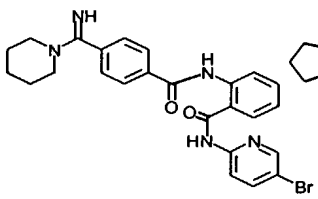
Example 63

MS (M+H): 468



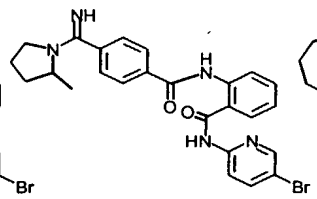
Example 64

MS (M+H): 492



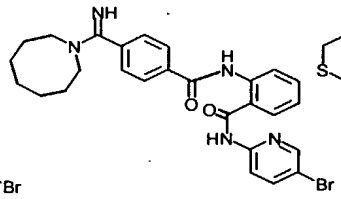
Example 65

MS (M+H): 506



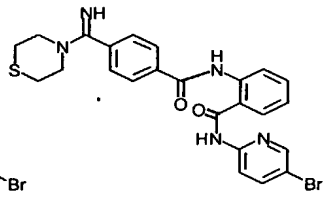
Example 66

MS (M+H): 506



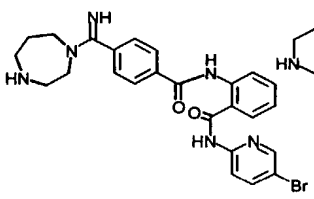
Example 67

MS (M+H): 520



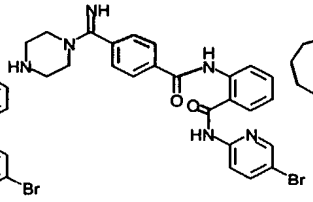
Example 68

MS (M+H): 524



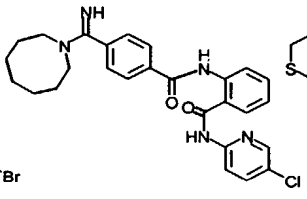
Example 69

MS (M+H): 521



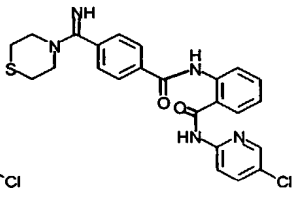
Example 70

MS (M+H): 507



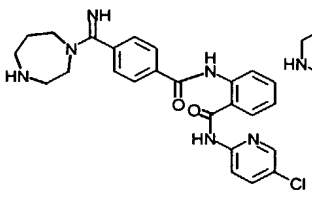
Example 71

MS (M+H): 476



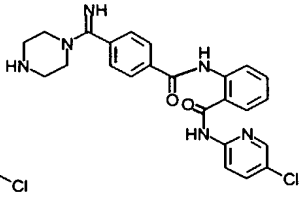
Example 72

MS (M+H): 480



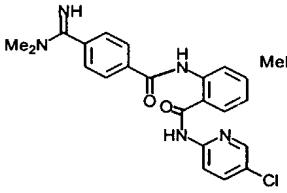
Example 73

MS (M+H): 477



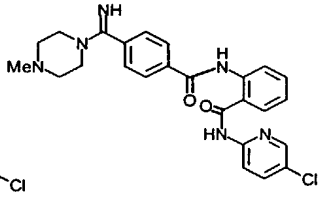
Example 74

MS (M+H): 463



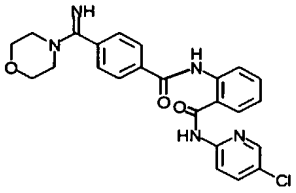
Example 75

MS (M+H): 422



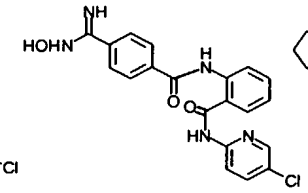
Example 76

MS (M+H): 477



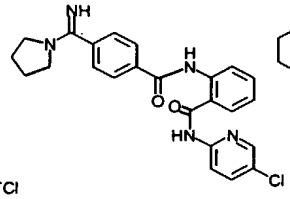
Example 77

MS (M+H): 464



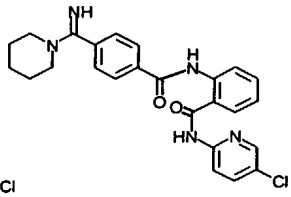
Example 78

MS (M+H): 410



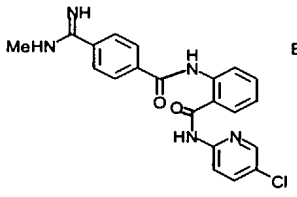
Example 79

MS (M+H): 448



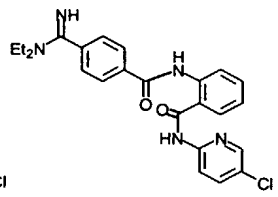
Example 80

MS (M+H): 462



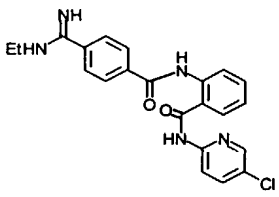
Example 81

MS (M+H): 408



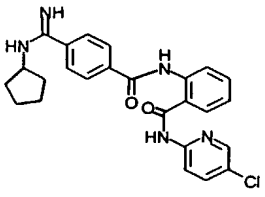
Example 82

MS (M+H): 22



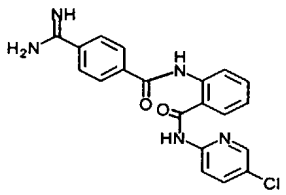
Example 83

MS (M+H): 450



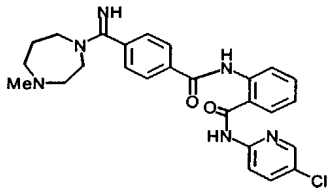
Example 84

MS (M+H): 462



Example 85

MS (M+H): 394

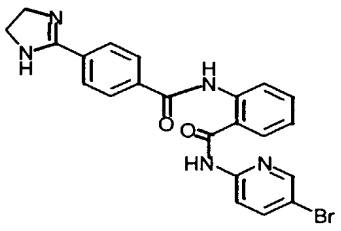


Example 86

MS (M+H): 491

Example 87

N-(5-bromo-2-pyridinyl)-(2-(4-(2-imidazolinyl)phenylcarbonyl)amino)-phenylcarboxamide.

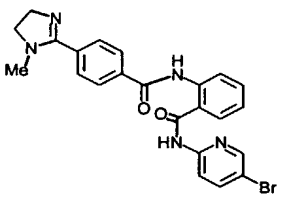


A stream of HCl(g) was bubbled through a 0°C solution of N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)-phenylcarboxamide (49 mg, 0.1 mmol) in 5 mL of methanol until saturation. The mixture was stirred at rt overnight and evaporated. The

resulting residue was treated with ethylene diamine (40 mg) in 10 ml methanol at reflux temperature for 2 h. The solvent was removed at reduced pressure and the crude benzamidine was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-(2-imidazolinyl)phenylcarbonyl)amino)-phenylcarboxamide (41 mg, 89%). MS found for $C_{22}H_{19}BrN_5O_2$ $(M+H)^+$: 464.

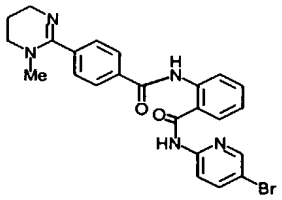
Examples 88-96

The following compounds of Examples 88-96 were prepared according to the procedure described in example 87.



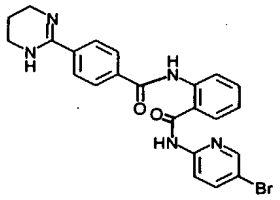
Example 88

MS (M+H): 478



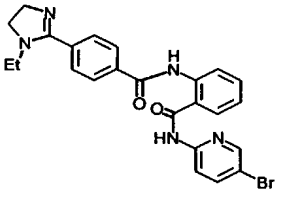
Example 89

MS (M+H): 492



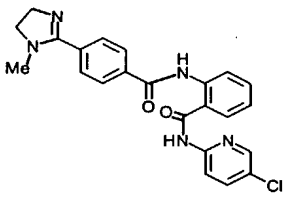
Example 90

MS (M+H): 478



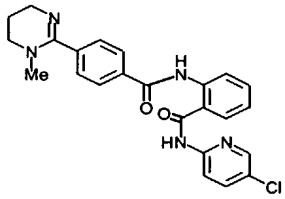
Example 91

MS (M+H): 492



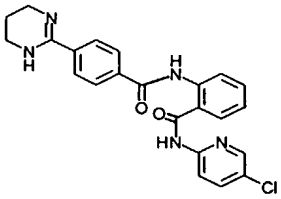
Example 92

MS (M+H): 434



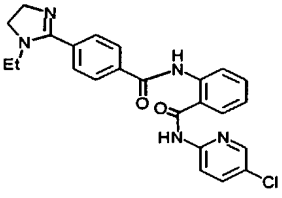
Example 93

MS (M+H): 448



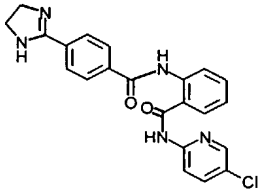
Example 94

MS (M+H): 434



Example 95

MS (M+H): 448

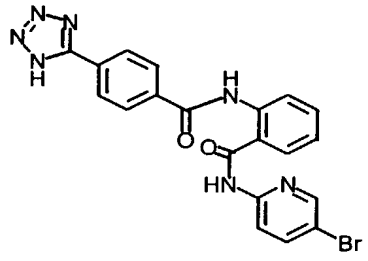


Example 96

MS (M+H): 420

Example 97

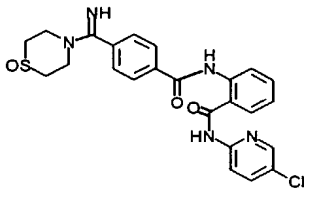
N-(5-bromo-2-pyridinyl)-(2-(4-(5-tetrazolyl)phenylcarbonyl)amino)-phenylcarboxamide.

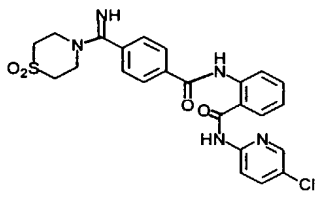


A mixture of N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)-phenylcarboxamide (49 mg, 0.1 mmol) and sodium azide (67 mg, 10 equiv) in 5 mL of DMF was heated at 100°C for 24h. The reaction mixture was diluted with EtOAc, washed with water, dried, filtered and evaporated. The residue was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-(5-tetrazolyl)phenylcarbonyl)amino)-phenylcarboxamide (33 mg, 65%). MS found for $C_{20}H_{15}BrN_7O_2$ $(M+H)^+$: 464.

Example 98 and Example 99

N-(5-bromo-2-pyridinyl)-(2-(4[-[1,1-doxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide and **N-(5-bromo-2-pyridinyl)-(2-(4-[1-oxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide.**

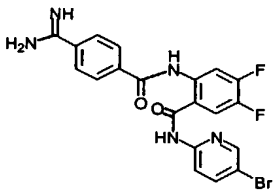




A mixture of N-(5-bromo-2-pyridinyl)-(2-(4-(1,4-thiazaperhydroin-4-yl)iminimethy]phenylcarbonyl)amino)-phenylcarboxamide (48 mg, 0.1 mmol) and and 3 mL of 30% hydrogen doxide was stirred at rt for 12h. The reaction was quenched with solid $Na_2S_2O_3$. Purification by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN gave N-(5-bromo-2-pyridinyl)-(2-(4[-[1,1-doxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide (15 mg, 31%), MS found for $C_{24}H_{23}ClN_5O_4S$ $(M+H)^+$: 512 and N-(5-bromo-2-pyridinyl)-(2-(4-[1-oxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide (20 mg, 41%). MS found for $C_{24}H_{23}ClN_5O_3S$ $(M+H)^+$: 496.

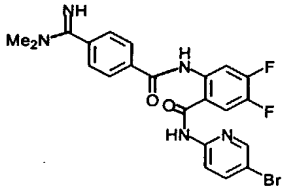
Examples 100-105

The following compounds were prepared according to the procedure described in example 56 and example 87.



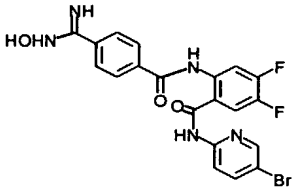
Example 100

MS (M+H): 474



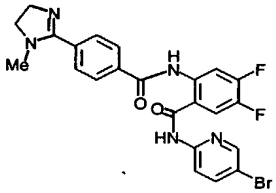
Example 101

MS (M+H): 502



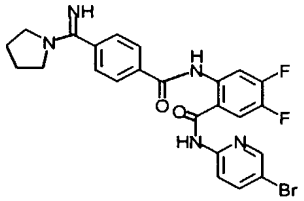
Example 102

MS (M+H): 490



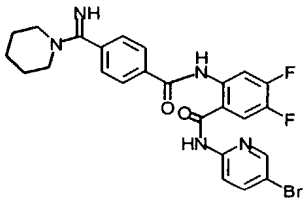
Example 103

MS (M+H): 514



Example 104

MS (M+H): 528

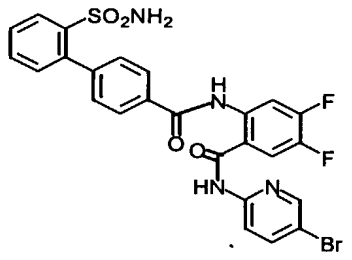


Example 105

MS (M+H): 542

Example 106

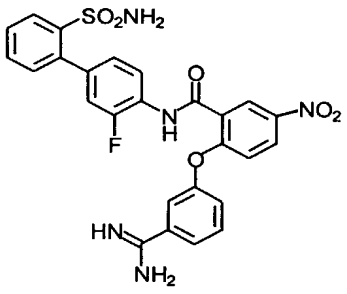
N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-4,5-difluorophenylcarboxamide.



This compound is prepared according to the procedure described in example 27. MS found for $C_{25}H_{18}BrF_2N_4O_4S$ $(M+H)^+$: 587.

Example 107

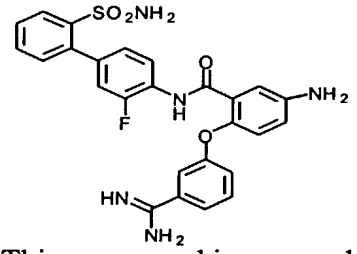
3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine.



This compound is prepared according to the procedure described in example 17. MS found for MS found for $C_{26}H_{21}FN_5O_6S$ $(M+H)^+$: 550.

Example 108

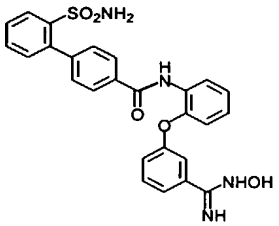
3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine.



This compound is prepared according to the procedure described in example 18. MS found for $C_{26}H_{23}FN_5O_4S$ $(M+H)^+$: 520.

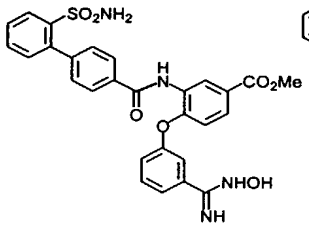
Examples 109-114

The following compounds were prepared according to the procedure described in example 1 except that in step 4, NH_2OH was used instead of NH_4OAc.



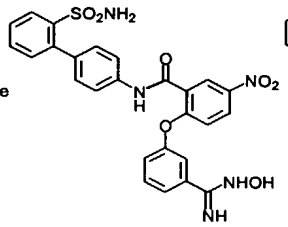
Example 109

MS (M+H): 502



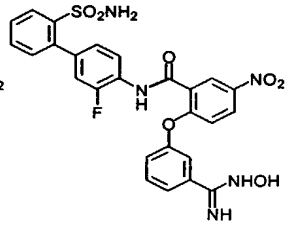
Example 110

MS (M+H): 560



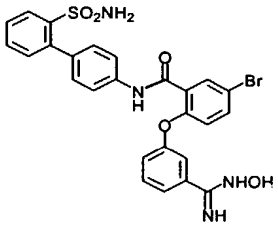
Example 111

MS (M+H): 547



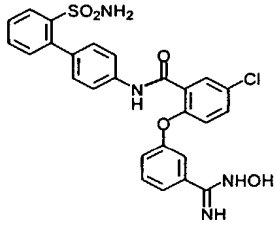
Example 112

MS (M+H): 547



Example 113

MS (M+H): 581

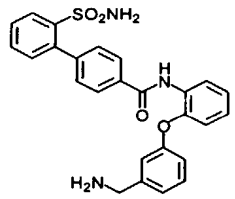


Example 114

MS (M+H): 537

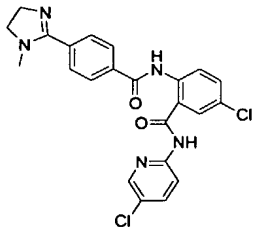
Example 115

3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzylamine.



A mixure of 3-(2-(4-[(2-t-butylaminosulfonyl)phenyl]benzoylamino)phenoxy)benzonitrile (53 mg, 0.1 mmol) (53 mg, 0.1 mmol, 1 equiv), 5 mg of Pd/C (10%) in 10 mL of methanol was stirred at rt under 1 atm H_2 atomosphere overnight. After filtration through a thin layer of Celite and removal of the volatile, residue was refluxed in 2 mL of TFA for 1h, and purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to 3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzylamine (13 mg, 27%). MS found for $C_{26}H_{24}N_3O_4S$ $(M+H)^+$: 474.

Example 116



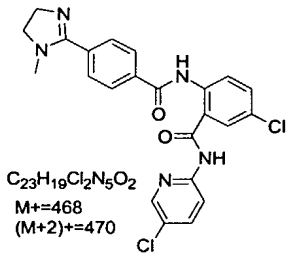
Step 1: To a solution of 2-amino-5-chloropyridine (328mg, 2.55mmol) in tetrahydrofuran (5ml) was 0.5M potassium bis(trimethylsilyl)amide in toluene (10ml, 5.05mmol) dropwise at –78 °C. After stirred for additional 0.5hr at –78 °C, the mixture was added 5-chloroisatoic anhydride (0.5g, 2.55mmol) at –78 °C. The mixture was warmed up to r.t gradually and stirred overnight. After quenched by saturated ammonium chloride solution, the mixture was extracted by ethyl acetate. The organic layer was dried over magnesium sulfate and concentrated to give (2-amino-5-chlorophenyl)-N-(5-chloro(2-pyridyl))carboxamide (0.71g. 100%). MS found for C12H9Cl2N3O M^+=282, $(M+2)^+$=284.

Step 2: To a solution of the compound of (2-amino-5-chlorophenyl)-N-(5-chloro(2-pyridyl))carboxamide (0.71g, 2.52mmol) in dichloromethane (10ml) was added 3-cyanobenzoly chloride (417mg, 2.52mmol) and pyridine (0.611ml, 7.55mmol). The mixture was stirred at r.t. overnight. The precipitate was filtered and washed with dichloromethane to give N-{4-chloro-2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-cyanophenyl)carboxamide as a solid (683mg, 66%). MS found for C20H12Cl2N4O2 M^+=411, $(M+2)^+$=413.

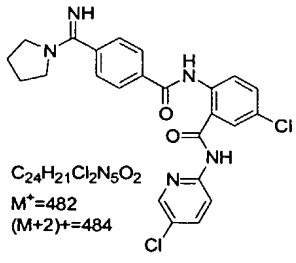
Step 3: To a solution of the compound of N-{4-chloro-2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-cyanophenyl)carboxamide (683mg, 1.66mmol) in anhydrous pyridine (10ml) and triethyl amine (1ml) was saturated with hydrogen sulfide gas at 0 °C. The mixture was stirred at r.t. overnight. After the evaporated the solvent, the residue was dissolved in anhydrous acetone (5ml) and iodomethane (1ml, 16.6mmol) was added. The mixture was stirred under reflux condition for 2 hrs. After the evaporation of solvent, the residue was dissolved in anhydrous methanol (5ml) and added a solution of N-methylethylenediamine (0.732ml, 8.3mmol) and acetic acid (1.5ml) in anhydrous methanol (5ml).The mixture was stirred under reflux condition for 2 hrs. After the evaporation of solvent, the crude residue was purified by RP-HPLC to give N-{4-chloro-2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide as a white powder. MS found for C23H19Cl2N5O2 M^+=468 $(M+2)^+$=470.

Examples 117-141

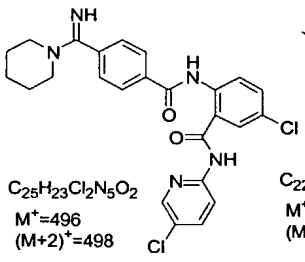
The following compounds were prepared according to the procedure described in example 116.



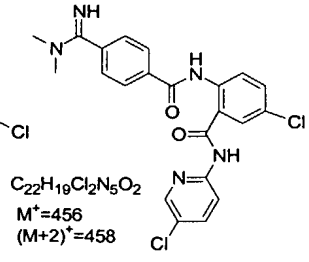
Example 117



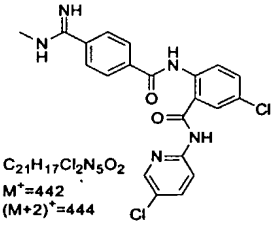
Example 118



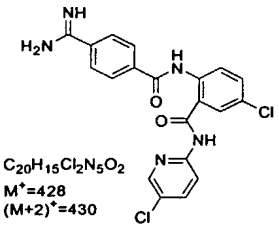
Example 119



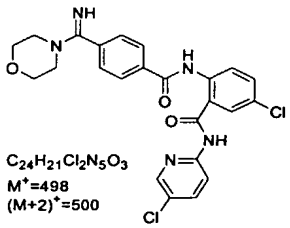
Example 120



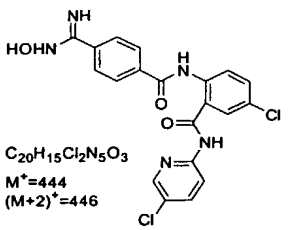
Example 121



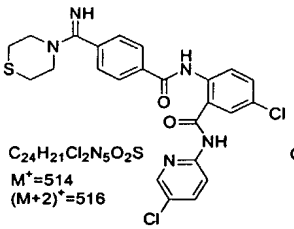
Example 122



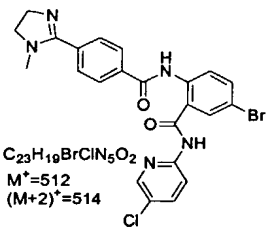
Example 123



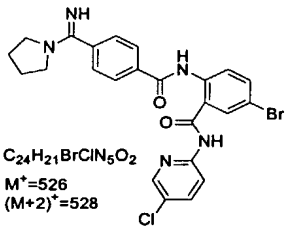
Example 124



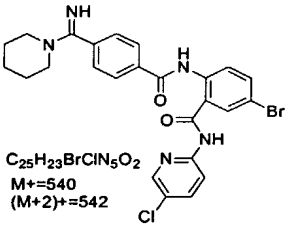
Example 125



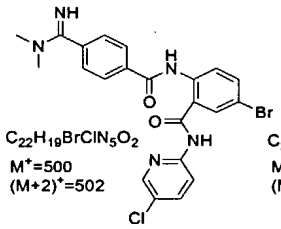
Example 126



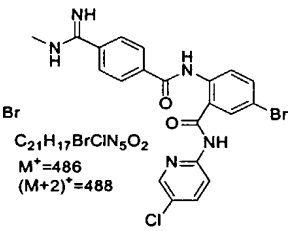
Example 127



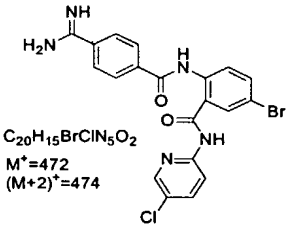
Example 128



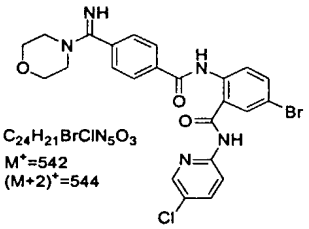
Example 129



Example 130

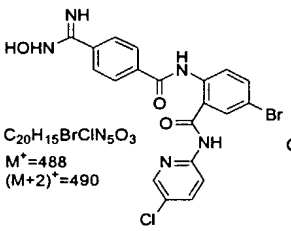


Example 131

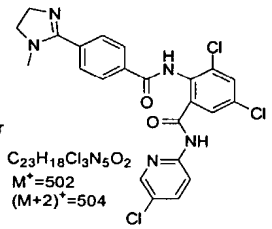


Example 132

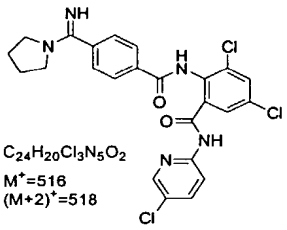
5



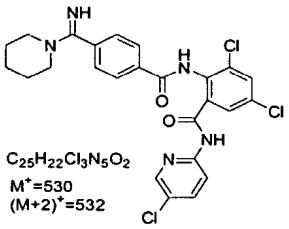
Example 133



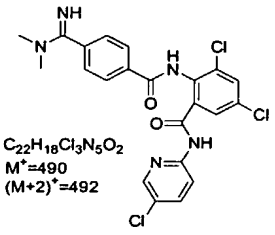
Example 134



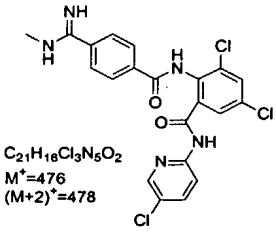
Example 135



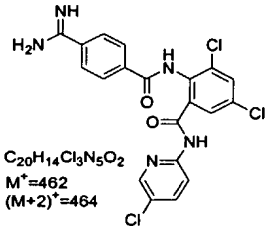
Example 136



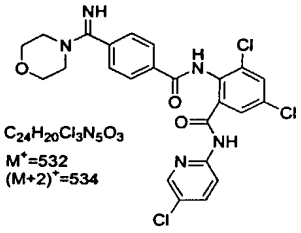
Example 137



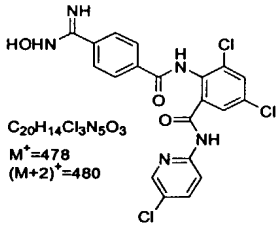
Example 138



Example 139

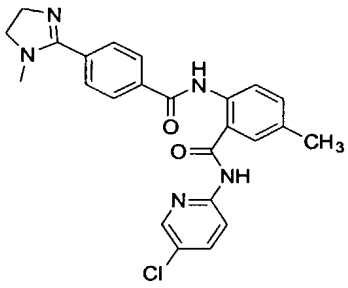


Example 140



Example 141

Example 142



Step 1: To a solution of 5-methyl-2-nitrobenzoic acid (1g, 5.52mmol) in dichloromethane (5ml) was added oxalyl chloride (0.964ml, 11.04mmol) and a few drops of dimethylformamide. The mixture was stirred at r.t. for 2 hrs. After the evaporation of the solvent, the residue was dissolved in dichloromethane (5ml). 2-amino-5-chloropyridine (852mg, 6.62mmol) and pyridine (1.34ml, 16.56mmol) were

added to the solution. The mixture was stirred at r.t. overnight. After the evaporation of the solvent, the crude residue was purified by silica gel column chromatography using solvent system 25% ethyl acetate in hexane as eluent to give N-(5-chloro(2-pyridyl))(5-methyl-2-nitrophenyl)carboxamide as a solid (1.48g, 92%). MS found for C13H10ClN3O3 M^+=291, $(M+2)^+$=293.

Step 2: To a solution of the compound of N-(5-chloro(2-pyridyl))(5-methyl-2-nitrophenyl)carboxamide (1.48g, 5.1mmol) in methanol (10ml) was added 5% Pt/C (1.48g, 0.19mmol). The mixture was applied hydrogen balloon at r.t.for 2 hrs. After the filtration by Celite, the filtrate was concentrated to give (2-aminophenyl)-N-(2-pyridyl)carboxamide, C, chloride, N (1.36g, 100%). MS found for C13H12ClN3O M^+=262, $(M+2)^+$=264.

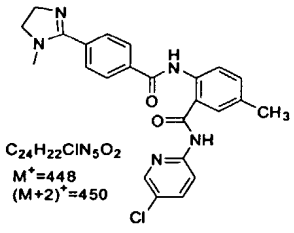
Step 3: To a solution of the compound of (2-aminophenyl)-N-(2-pyridyl)carboxamide, C, chloride, N (1.36g, 5.2mmol) in dichloromethane (10ml) was added 3-cyanobenzoly chloride (860mg, 5.2mmol) and pyridine (1.26ml, 15.6mmol). The mixture was stirred at r.t. overnight. After the evaporation of the solvent, the crude residue was purified by silica gel column chromatography using solvent system 25% ethyl acetate in hexane as eluent to give N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methylphenyl}(4-cyanophenyl)carboxamide as a solid (830mg, 41%). MS found for C21H15ClN4O2 M^+=390, $(M+2)^+$=392.

Step 4: To a lotion of the compound of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methylphenyl}(4-cyanophenyl)carboxamide (830mg, 2.1mmol) in anhydrous methanol (5ml) and ethyl acetate (10ml) was saturated with hydrogen chloride gas at 0 °C. The mixture was stirred at r.t. overnight. After the evaporated the solvent, the residue was dissolved in anhydrous methanol (5ml) and N-methylethylenediamine (0.926ml, 10.5mmol) was added. The mixture was stirred under reflux condition for 2 hrs. After the evaporation of solvent, the crude residue was purified by RP-HPLC to give N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methylphenyl}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide as a white powder. MS found for C24H22ClN5O2 M^+=448, $(M+2)^+$=450.

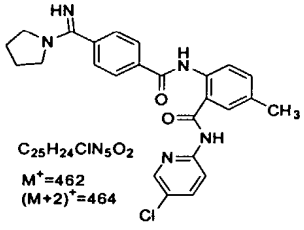
Examples 143-148

The following compounds were prepared according to the procedure described in Example 142.

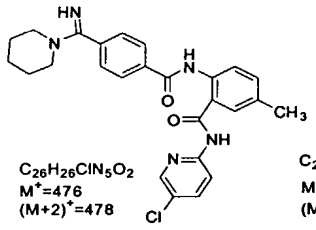
5



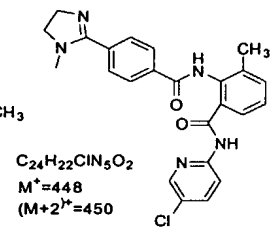
Example 143



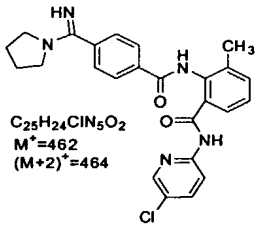
Example 144



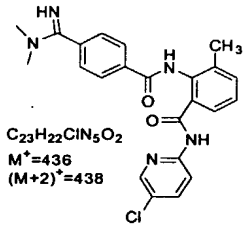
Example 145



Example 146

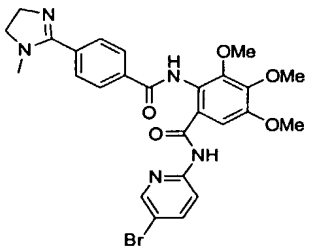


Example 147



Example 148

Example 149



Step 1: To a solution of 3,4,5-trimethoxy-2-nitrobenzoic acid (0.5g, 1.95mmol) in dichloromethane (5ml) was added oxalyl chloride (0.34ml, 3.9mmol) and a few drops of dimethylformamide. The mixture was stirred at r.t. for 2 hrs. After the evaporation of the solvent, the residue was dissolved in dichloromethane (5ml). 2-amino-5-bromopyridine (0.81g, 4.7mmol) and pyridine (0.94ml, 11.7mmol) were added to the solution. The mixture was stirred at r.t. overnight. After the evaporation of the solvent, the crude residue was purified by silica gel column chromatography using solvent system 25% ethyl acetate in hexane as eluent to give N-(5-bromo(2-pyridyl))(3,4,5-trimethoxy-2-nitrophenyl)carboxamide as a solid (790mg, 98%). MS found for C15H14BrN3O6 M^+=412, $(M+2)^+$=414.

Step 2: To a solution of the compound of N-(5-bromo(2-pyridyl))(3,4,5-trimethoxy-2-nitrophenyl)carboxamide (790mg, 1.92mmol) in ethyl acetate (5ml) was added tin chloride (II) hydrate (1.73g, 7.67mmol). The mixture was stirred under reflux condition for 2 hrs. After filtered by Celite, the filtrate was added 1N sodium hydroxide solution and extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and concentrated to give (2-amino-3,4,5-trimethoxyphenyl)-N-(5-bromo(2-pyridyl))carboxamide (570mg, 77%). MS found for C15H16BrN3O4 M^+=382, $(M+2)^+$=384.

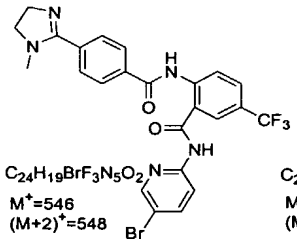
Step 3: To a solution of the compound of (2-amino-3,4,5-trimethoxyphenyl)-N-(5-bromo(2-pyridyl))carboxamide (570mg, 1.49mmol) in dichloromethane (5ml) was added 3-cyanobenzoly chloride (247mg, 1.49mmol) and pyridine (0.362ml, 4.48mmol). The mixture was stirred at r.t. overnight. After the evaporation of the solvent, the crude residue was purified by silica gel column chromatography using

solvent system 25% ethyl acetate in hexane as eluent to give N-{6-[N-(5-bromo(2-pyridyl))carbamoyl]-2,3,4-trimethoxyphenyl}(4-cyanophenyl)carboxamide as a solid (680mg, 69%). MS found for C23H19BrN4O5 M^+=511, $(M+2)^+$=513.

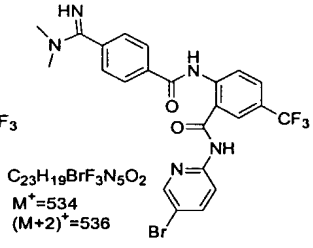
Step 4: To a slotion of the compound of N-{6-[N-(5-bromo(2-pyridyl))carbamoyl]-2,3,4-trimethoxyphenyl}(4-cyanophenyl)carboxamide (680mg, 1.33mmol) in anhydrous methanol (5ml) and ethyl acetate (10ml) was saturated with hydrogen chloride gas at 0 °C. The mixture was stirred at r.t. overnight. After the evaporated the solvent, the residue was dissolved in anhydrous methanol (5ml) and N-methylethylenediamine (0.586ml, 6.65mmol) was added. The mixture was stirred under reflux condition for 2 hrs. After the evaporation of solvent, the crude residue was purified by RP-HPLC to give N-{6-[N-(5-bromo(2-pyridyl))carbamoyl]-2,3,4-trimethoxyphenyl}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide as a white powder (240mg, 32%). MS found for C26H26BrN5O5 M^+=568, $(M+2)^+$=570.

Examples 150-153

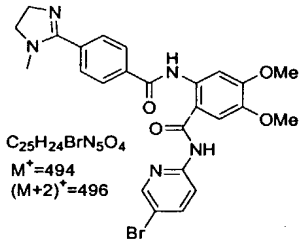
The following compounds were prepared according to the procedure described in Example 149.



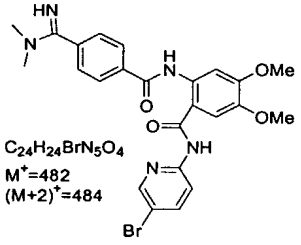
Example 150



Example 151

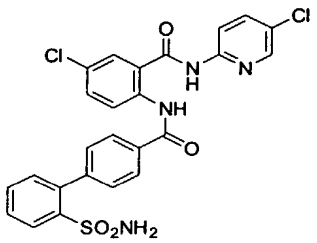


Example 152



Example 153

Example 154



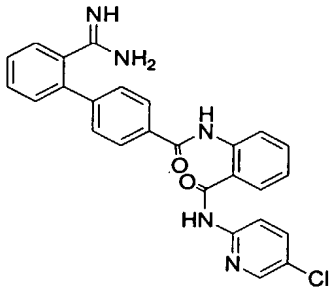
Step 1: To a solution of 4-{2-{[(tert-butyl)amino}sulfonyl}phenyl}benzoic acid (167mg, 0.5mmol) in dichloromethane (5ml) was added oxalyl chloride (0.09ml, 1mmol) and a few drops of dimethylformamide. The mixture was stirred at r.t. for 2 hrs. After the evaporation of the solvent, the residue was dissolved in dichloromethane (5ml). The compound of (2-amino-5-chlorophenyl)-N-(5-chloro(2-pyridyl))carboxamide (0.17g, 0.6mmol) and pyridine (0.122ml, 1.5mmol) were added to the solution. The mixture was stirred at r.t. overnight. The solvent was evaporated to give (2-{[4-(2-{[(tert-butyl)amino]sulfonyl}phenyl)phenyl]-carbonylamino}-5-chlorophenyl)-N-(5-chloro(2-pyridyl))carboxamide. MS found for C29H26Cl2N4O4S M^+=597, $(M+2)^+$=599.

Step 2: The mixture of the compound of (2-{[4-(2-{[(tert-butyl)amino]sulfonyl}phenyl)phenyl] carbonylamino}-5-chlorophenyl)-N-(5-chloro(2-pyridyl))carboxamideexample 12 (0.5mmol) in trifluoroacetic acid (5ml) was stirred at r.t. for 5hrs. After the evaporation of solvent, the crude residue was purified by RP-HPLC to give

N-(5-chloro(2-pyridyl))(5-chloro-2-{[4-(2-sulfamoylphenyl)-phenyl]carbonylamino}phenyl)-carboxamide as a white powder (68mg, 25%). MS found for C25H18Cl2N4O4S
M^+=541, $(M+2)^+$=543.

Example 155

2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]-benzenecarboxamidine

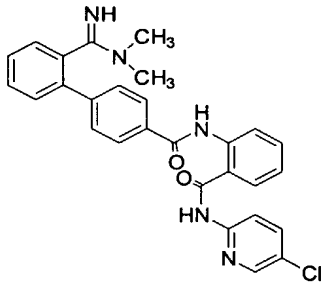


$C_{26}H_{20}ClN_5O_2$
Exact Mass: 469.13
Mol. Wt.: 469.92

A stream of H_2S (g) was bubbled through a 0 °C solution of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} [4-(2-cyanophenyl)phenyl]carboxamide (100 mg, 0.22 mmol, 1.0 equiv.) in 9 mL pyridine and 1 mL NEt_3 until saturation. The mixture was stirred at rt for 1 day and evaporated. The resulting residue was treated with MeI (94 mg, 0.663 mmol, 3.0 equiv.) in 10 mL acetone at reflux temperature for 1 hr and concentrated to dryness. The resulting residue was treated with a mixture of NH_4OAc (340 mg, 4.42 mmol, 20 equiv.) in 0.5 mL acetic acid and 2 mL methanol at 50 °C for 2 days. The solvent was removed at reduced pressure and the crude benzamidine was purified by HPLC (C18 reversed phase) eluting with 0.1% TFA in H_2O/CH_3CN to give 2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]benzenecarboxamidine (15 mg, 15%). MS found for $C_{26}H_{20}ClN_5O_2$ $(M+H)^+$: 470.

Example 156

(4-{2-[(dimethylamino)iminomethyl]phenyl}phenyl)-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide

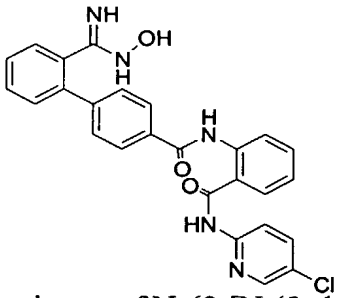


$C_{28}H_{24}ClN_5O_2$
Exact Mass: 497.16
Mol. Wt.: 497.98

This compound was prepared according to the procedure described in Example 155.
MS found for $C_{28}H_{24}ClN_5O_2$ $(M+H)^+$: 498.

Example 157

N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}{4-[2-((hydroxyamino)iminomethyl)-phenyl]phenyl}carboxamide

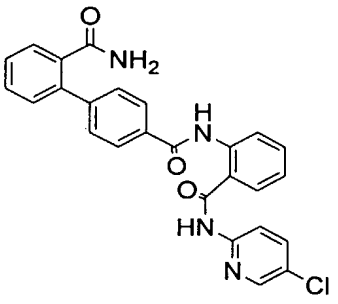


$C_{26}H_{20}ClN_5O_3$
Exact Mass: 485.13
Mol. Wt.: 485.92

A mixture of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}[4-(2-cyanophenyl)phenyl] carboxamide (14 mg, 0.03 mmol, 1.0 equiv.), hydroxyamine hydrochloride (6.25 mg, 0.09 mmol, 3.0 equiv.) and triethyl amine (0.03 mL, 0.3 mmol, 10.0 equiv.) in ethanol (3 mL) was stirred at rt for 6 days, concentrated and HPLC (C18 reversed phase) eluting with 0.1% TFA in H_2O/CH_3CN to give N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[2-((hydroxyamino)iminomethyl) phenyl] phenyl}carboxamide (4 mg, 27.5%).
MS found for $C_{26}H_{20}ClN_5O_3$ $(M+H)^+$: 486.

Example 158

2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]benzamide

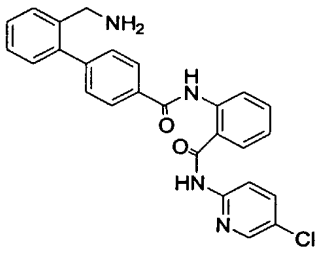


$C_{26}H_{19}ClN_4O_3$
Exact Mass: 470.11
Mol. Wt.: 470.91

This compound was ontained as on of the side product in Example 157.
MS found for $C_{26}H_{19}ClN_4O_3$ $(M+H)^+$: 471

Example 159

{4-[2-(aminomethyl)phenyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-phenyl}carboxamide

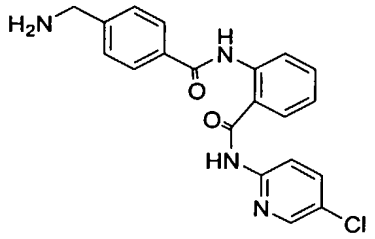


$C_{26}H_{21}ClN_4O_2$
Exact Mass: 456.14
Mol. Wt.: 456.92

A mixture of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}[4-(2-cyanophenyl)phenyl] carboxamide (200 mg, 0.442 mmol, 1.0 equiv.), cobalt chloride (86 mg, 0.664 mmol, 1.5 equiv.) and sodium borohydride (50 mg, 1.33 mmol, 3.0 equiv.) in DMF (15 mL) was stirred at 0 ^{0}C to rt for 3 days. The reaction was quenched with ice cubes, diluted with DCM (100 mL) and filtered through celite. The filtrate was washed with saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered, evaporated and HPLC (C18 reversed phase) eluting with 0.1% TFA in H_2O/CH_3CN gave {4-[2-(aminomethyl)phenyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide (87 mg, 43%). MS found for $C_{26}H_{21}ClN_4O_2$ $(M+H)^+$: 457.

Example 160

[4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide

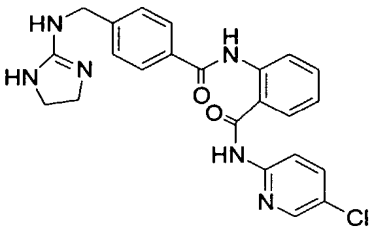


$C_{20}H_{17}ClN_4O_2$
Exact Mass: 380.10
Mol. Wt.: 380.83

A mixture of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-cyanophenyl)carboxamide (1 g, 2.6 mmol, 1.0 equiv.), cobalt chloride (0.5 g, 3.85 mmol, 1.5 equiv.) and sodium borohydride (0.295 g, 7.8 mmol, 3.0 equiv.) in DMF (20 mL) was stirred at 0 °C to rt for 2.5 hr. The reaction was quenched with ice cubes, diluted with ethyl acetate (100 mL) and filtered through celite. The filtrate was washed with saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered, evaporated and HPLC (C18 reversed phase) eluting with 0.1% TFA in H_2O/CH_3CN gave [4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide (320 mg, 30%). MS found for $C_{20}H_{17}ClN_4O_2$ $(M+H)^+$: 381.

Example 161

N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}{4-[(2-imidazolin-2-ylamino)methyl]-phenyl}carboxamide

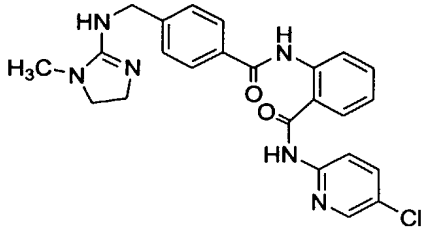


$C_{23}H_{21}ClN_6O_2$
Exact Mass: 448.14
Mol. Wt.: 448.90

A mixture of [4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide (80 mg, 0.21 mmol), 2-methylthio-2-imidazoline hydriodide (77 mg, 0.315 mmol, 1.5 equiv.) and triethyl amine (0.5 mL) in 1 mL DMF was stirred at room temperature overnight, concentrated to dryness and HPLC (C18 reversed phase) eluting with 0.1% TFA in H_2O/CH_3CN gave N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[(2-imidazolin-2-ylamino)methyl]phenyl}carboxamide (13.5 mg, 15%). MS found for $C_{23}H_{21}ClN_6O_2$ $(M+H)^+$: 449

Example 162

N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-{[(1-methyl(2-imidazolin-2-yl))amino]methyl}phenyl)carboxamide



$C_{24}H_{23}ClN_6O_2$
Exact Mass: 462.16
Mol. Wt.: 462.93

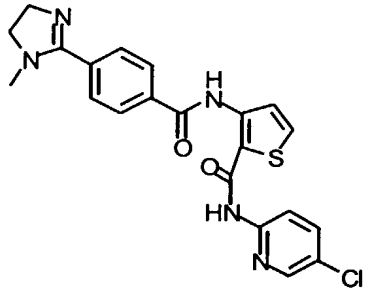
Step 1: To the boiling solution of 2-methylthio-2-imidazoline hydriodide (1 g, 8.4 mmol) in methanol (10 mL) was added MeI (0.78 mL, 12.6 mmol, 1.5 equiv.) dropwise. The reaction mixture was stirred at reflux temperature for 1 hr, concentrated and crystallized with ether to give 1-methyl-2-methylthio-2-imidazoline (1.1 g, 100%).
MS found for $C_5H_{10}N_2S$ $(M+H)^+$: 131.

Step 2: A mixture of [4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide (74 mg, 0.195 mmol), 1-methyl-2-methylthio-2-imidazoline (25 mg, 0.195 mmol), NEt3 (2 mL) and pyridine (5 mL) was stirred at 80 ^{0}C overnight, concentrated and HPLC (C18 reversed phase)eluting with 0.1% TFA in H2O/CH3CN gave N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-{[(1-methyl(2-imidazolin-2-

yl))amino]methyl}phenyl)carboxamide (52 mg, 65%). MS found for $C_{24}H_{23}ClN_6O_2$ $(M+H)^+$: 463.

Example 163

N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide



Preparation of methyl 3-[(4-cyanophenyl)carbonylamino]thiophene-2-carboxylate

A mixture of 4-cyanobenzoyl chloride (1.0500g, 6.4 mmol), methyl 3-aminothiophenecarboxylate (1.0000g, 6.4 mmol), and triethylamine (1 mL, 7.0 mmol) in dichloromethane was stirred at room temperature for 18 hours. The mixture was poured into a separatory funnel and washed by 1 N HCl. The organic layers were combined, dried over MgSO4, concentrated in *vacuo*, and chromatographed through a silica gel column to give the title compound 1.6588 g (91%). ES-MS 287 (M+1).

Preparation of N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}(4-cyanophenyl)carboxamide

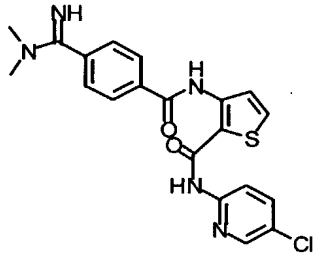
A portion of 2-amino-5-chloropyridine (68.6 mg, 0.5 mmol) was treated with AlMe3 (0.8 mL, 1.6 mmol), followed by adding the product from step A (160 mg, 0.5 mmol). The mixture was stirred at room temperature for 18 hours. The excess of AlMe3 was killed by 1N HCl solution. The organic layers were combined, dried over MgSO4, concentrated in *vacuo*, and chromatographed through a silica gel column to give the title compound 0.1528 g (80%). ES-MS 383 (M+1).

Preparation of Example 163.

A mixture of the product from step B (0.1528 g, 0.4 mmol) and EtOH saturated with HCl was stirred at room temperature for 18 hours. The solvent was removed by a rotovap. The crude oil was treated with 2 mL N-methylethylenediamine for 2 hours until the reaction was complete. Prep HPLC was used to purity the final product. It gave 0.1537 g (88%). ES-MS 440(M+1).

Example 164

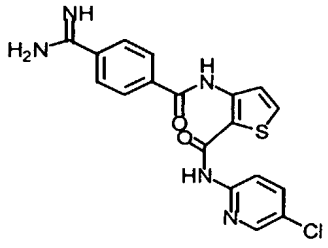
{4-[(dimethylamino)iminomethyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide



Example 164 was made by the procedure of Example 163. ES-MS 428(M+1).

Example 165

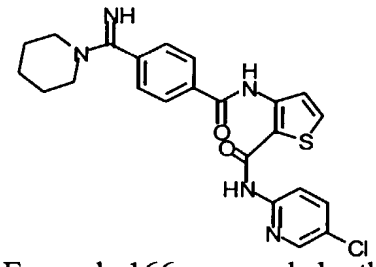
4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine



Example 165 was made by the procedure of Example 163. ES-MS 400(M+1).

Example 166

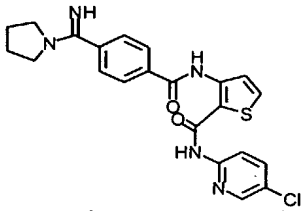
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopiperidylmethyl)-phenyl]carboxamide



Example 166 was made by the procedure of Example 163. ES-MS 468(M+1).

Example 167

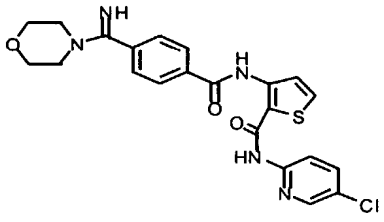
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopyrrolidinylmethyl)-phenyl]carboxamide



Example 167 was made by the procedure of Example 163. ES-MS 454(M+1).

Example 168

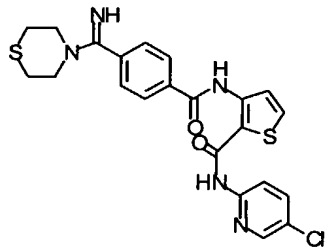
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminomorpholin-4-ylmethyl)phenyl]carboxamide



Example 168 was made by the procedure of Example 163. ES-MS 470(M+1).

Example 169

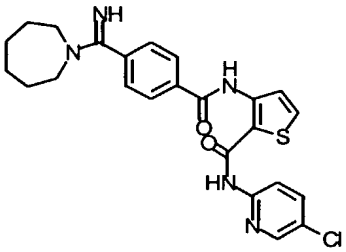
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carboxamide



Example 169 was made by the procedure of Example 163. ES-MS 486(M+1).

Example 170

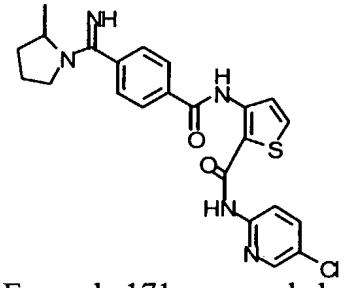
[4-(azaperhydroepinyliminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide



Example 170 was made by the procedure of Example 163. ES-MS 482(M+1).

Example 171

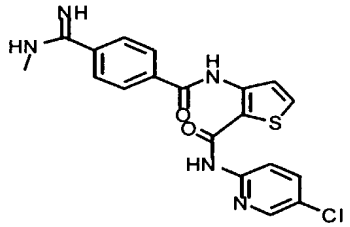
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}{4-[imino(2-methylpyrrolidinyl)methyl]phenyl}carboxamide



Example 171 was made by the procedure of Example 163. ES-MS 468(M+1).

Example 172

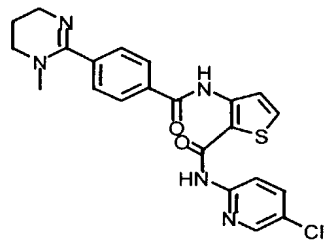
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}{4-[imino(methylamino)methyl]-phenyl}carboxamide



Example 172 was made by the procedure of Example 163.

Example 173

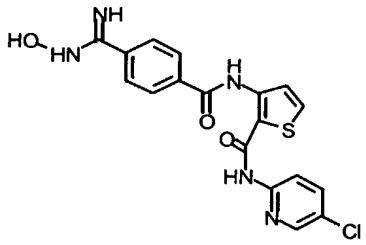
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(3-methyl(3,4,5,6-tetrahydropyrimidin-2-yl))phenyl]carboxamide



Example 173 was made by the procedure of Example 163. ES-MS 414(M+1).

Example 174

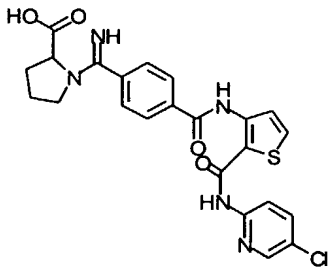
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-((hydroxyamino)iminomethyl)-phenyl]carboxamide



Example 174 was made by the procedure of Example 163. ES-MS 416(M+1).

Example 175

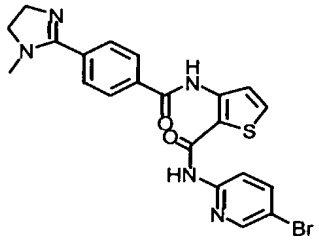
1-{[4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carbamoyl)phenyl]-iminomethyl}pyrrolidine-2-carboxylic acid



Example 175 was made by the procedure of Example 163. ES-MS 498(M+1).

Example 176

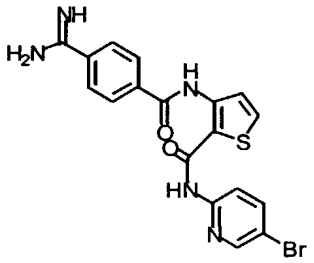
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide



Example 176 was made by the procedure of Example 163. ES-MS 484(M+1).

Example 177

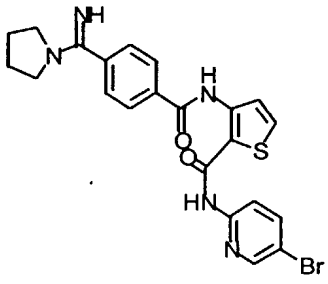
4-(N-{2-[N-(5-bromo-2-pyridyl)carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine



Example 177 was made by the procedure of Example 163. ES-MS 444(M+1).

Example 178

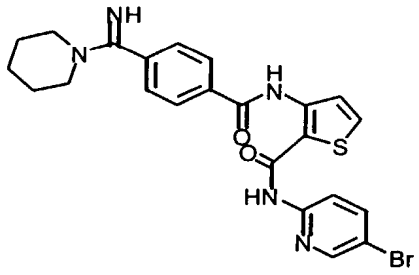
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopyrrolidinylmethyl)phenyl]carboxamide



Example 178 was made by the procedure of Example 163. ES-MS 494(M+1).

Example 179

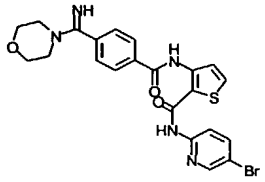
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopiperidylmethyl)phenyl]carboxamide



Example 179 was made by the procedure of Example 163. ES-MS 512(M+1).

Example 180

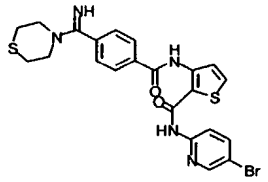
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminomorpholin-4-ylmethyl)phenyl]carboxamide



Example 180 was made by the procedure of Example 163. ES-MS 514(M+1).

Example 181

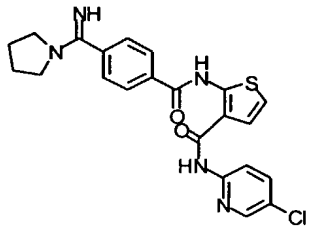
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carboxamide



Example 181 was made by the procedure of Example 163. ES-MS 530(M+1).

Example 182

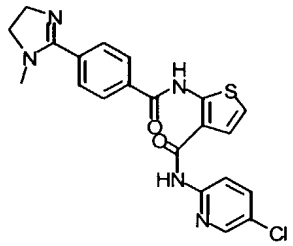
N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl)}[4-(iminopyrrolidinylmethyl)phenyl]carboxamide



Example 182 was made by the procedure of Example 163. ES-MS 454(M+1).

Example 183

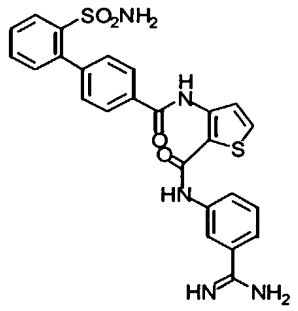
N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide



Example 183 was made by the procedure of Example 163. ES-MS 440(M+1).

Example 184

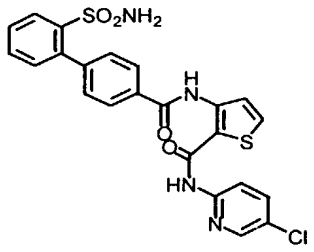
3-[(3-{[4-(2-sulfamoylphenyl)phenyl]carbonylamino}-2-thienyl)carbonylamino]benzenecarboxamidine



Example 184 was made by the procedure of Example 163 (step A, B, C) followed by a final step of trifluoroacetic acid removal of the *t*-butyl group. 4-(2-{[(tert-butyl)amino]sulfonyl}phenyl)benzoyl chloride was used to replace 4-cyanobenzoyl chloride in Example 1. ES-MS 520(M+1).

Example 185

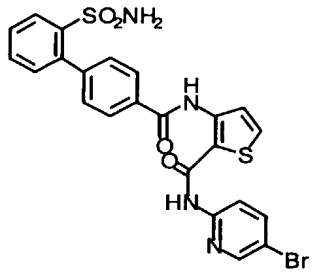
N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(2-sulfamoylphenyl)phenyl]carboxamide



Example 185 was made by the procedure of Example 163 except using 4-(2-{[(tert-butyl)amino]sulfonyl}phenyl)benzoyl chloride instead of 4-cyanobenzoyl chloride. ES-MS 513(M+1).

Example 186

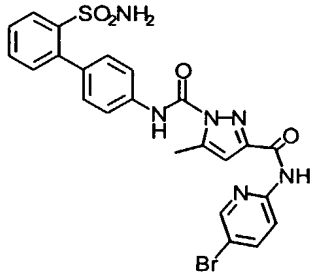
N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(2-sulfamoylphenyl)phenyl]carboxamide



Example 186 was made by the procedure of Example 185. ES-MS 556(M+1).

Example 187

N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl)5-methyl-pyrazolcarboxamide.



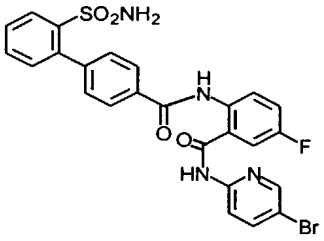
Step 1: A solution of 2-amino-5-bromopyridine (0.200 g, 1.16 mmol 1.0 equiv), in 5 mls of methylene chloride, under argon, was treated with trimethylaluminum (0.312 mL, 2.0N in hexanes, 4.0 equiv) at room temperature for 30 min. To the solution was added ethyl-3-methylpyrazole-5-carboxylate (0.356 g, 2.0 equiv). After 4hrs, the volatile was evaporated, and the residue was redissolved into EtOAc, washed with

0.5N HCl, 0.2 N K_2CO_3, and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, evaporated and purified via flash chromatography on silica gel to give N-(5-bromo-2-pyridinyl)-(3-methyl)5-pyrazolecarboxamide (0.160 g, 49%). MS found for $C_{10}H_9BrN_4O$ $(M+H)^+$: 281, 283.

Step 2: A solution of N-(5-bromo-2-pyridinyl)-(3-methyl)5-pyrazolecarboxamide (0.060 g, 0.213 mmol, 1.0 equiv) in 2 mL of acetonitrile was treated with triphosgene (0.063 g, 1.0 equiv) at room temperature for 5min under argon. To the solution was added 4-[(2-t-butylaminosulfonyl)phenyl]phenylamine (0.071 g, 1.1 equiv) After 1 hr, the volatile was evaporated and the residue was redissolved into EtOAc, washed with 0.5N HCl, 0.2 N K_2CO_3, and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, evaporated, purified via flash chromatography on silica gel and then reacted in 2 mL of trifluoroacetic acid for 16 hrs at room temperature. TFA was then evaporated and the residue was redissolved into EtOAc, washed with 0.5N HCl, 0.2 N K_2CO_3, and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, evaporated, and triturated with diethyl ether to give N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl] phenylaminocarbonyl)5-methyl-pyrazolcarboxamide (0.0024 g, 2%). MS found for $C_{23}H_{19}BrN_6O_4S$ $(M+H)^+$: 555, 557.

Example 188

N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-5-fluorophenylcarboxamide.



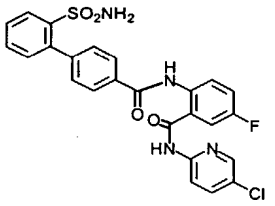
Step 1: A solution of 5-fluoro-2-nitrobenzoic acid (10.0 g, 54 mmol, 1.0 equiv), 2-amino-5-bromopyridine (12.2 g, 1.3 equiv), in 80 mL of pyridine was treated with phosphorous oxychloride (25.3 g, 3.0 equiv) for 30 min. The volatile was evaporated

and the residue was redissolved into EtOAc, washed with 1N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated. The volatile was evaporated, and the product was triturated with diethyl ether to give N-(5-bromo-2-pyridinyl)-(2-nitro)-5-fluorophenylcarboxamide (12.5 g, 68%). MS found for $C_{12}H_7BrFN_3O_3$ $(M+H)^+$: 340, 342.

Step 2: A solution of N-(5-bromo-2-pyridinyl)-(2-nitro)-5-flurophenylcarboxamide (2.0 g, 5.88 mmol, 1.0 equiv) in 30 mL of EtOAc was treated with $SnCl_2 2H_2O$ (5.90 g, 4 equiv) at reflux for 4 h. The volatile was evaporated and the residue was redissolved in EtOAc, washed with saturated aqueous $NaHCO_3$ and 1N NaOH. The organic layer was dried over $MgSO_4$, filtered and evaporated to N-(5-bromo-2-pyridinyl)-(2-amino)-5-fluorophenylcarboxamide (1.79 g, 98%). MS found for $C_{12}H_9BrFN_3O$ $(M+H)^+$: 310, 312.

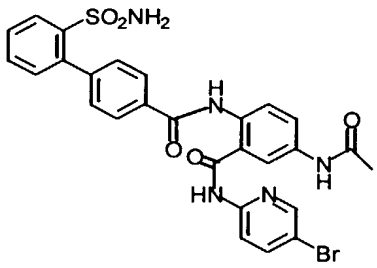
Step 3: A mixture of N-(5-bromo-2-pyridinyl)-(2-amino)-5-fluorophenylcarboxamide (0.310 g, 1 mmol, 1.0 equiv), 4-[(2-t-butylaminosulfonyl)phenyl]benzoyl chloride (0.430 g, 1.3 equiv), pyridine (2 mL) in 10 mL of dichloromethane was stirred at rt overnight The volatile was evaporated and the residue was redissolved into EtOAc, washed with 1N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated. The intermediate was reacted into 5 mL of trifluoroacetic acid at rt overnight. TFA was then evaporated and the product was triturated with diethyl ether, and then with chloroform to give N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl] phenylcarbonylamino)-5-fluorophenylcarboxamide (120 mg, 21%). MS found for $C_{25}H_{18}BrFN_4O_4S$ $(M+H)^+$: 569, 571.

Example 189



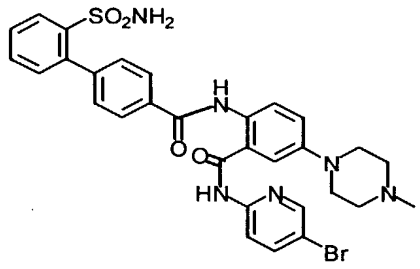
This compound is prepared according to the procedure described in example 2 with the exception of using zinc in acetic acid to reduce nitro-intermediate in step 2. The final product was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN. MS found for $C_{25}H_{18}ClFN_4O_4S$ $(M+H)^+$: 525, 527.

Example 190



This compound is prepared according to the procedure described in example 2 with the exception of using 5-acetamido-2-nitrobenzoic acid as the starting material in step 1. The final product was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN MS found for $C_{27}H_{22}BrN_5O_5S$ $(M+H)^+$: 608, 610.

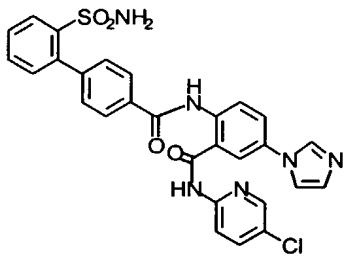
Example 191



This compound is prepared according to the procedure described in example 2 with the exception of the following step 1b performed on the nitro-intermediate from step 1. The final product was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN MS found for $C_{30}H_{29}BrN_6O_4S$ $(M+H)^+$: 649, 651.

Step 1b: A mixture of N-(5-bromo-2-pyridinyl)-(2-nitro)-5-fluorophenylcarboxamide (0.68 g, 2 mmol, 1.0 equiv), N-methylpiperazine (0.60 g, 3 equiv), and Cs_2CO_3 (1.30 g, 2 equiv) in 5 mL of dimethylformamide was stirred at 90°C overnight. Ethyl acetate was added and washed with H_2O. The organic layer was dried over Na_2SO_4, filtered, evaporated, purified via flash chromatography on silica gel to give N-(5-bromo-2-pyridinyl)-(2-nitro)-5-(4-N-methylpiperazine)phenylcarboxamide (0.54g, 65%). MS found for $C_{17}H_{18}BrN_5O_3$ $(M+H)^+$: 419, 421.

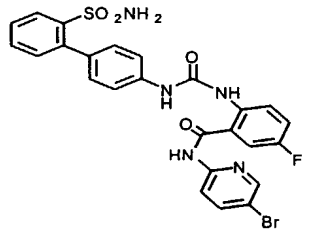
Example 192



This compound is prepared according to the procedure described in example 5. The final product was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN MS found for $C_{28}H_{21}ClN_6O_4S$ $(M+H)^+$: 573, 575.

Example 193

N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonylamino)-5-fluorophenylcarboxamide.

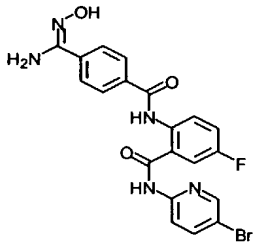


Step 3: A mixture of 4-[(2-t-butylaminosulfonyl)phenyl]phenylamine (0.180 g, 1.2 equiv), N,N'-disuccinimidyl carbonate (0.154 g, 1.2 equiv), 4-methylmorpholine (0.5

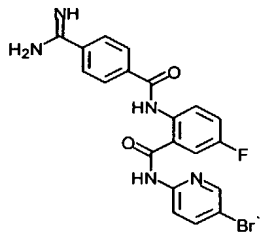
mL) in 10 mL of acetonitrile was stirred at rt for 30 min. N-(5-bromo-2-pyridinyl)-(2-amino)-5-fluorophenylcarboxamide (0.155 g, 0.5 mmol, 1.0 equiv) was added and the solution was stirred at rt for 3 hrs. The volatile was evaporated and the residue was redissolved into EtOAc, washed with 1N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated. The intermediate was reacted into 5 mL of trifluoroacetic acid at rt overnight. TFA was then evaporated and the product was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl] phenylaminocarbonylamino)-5-fluorophenylcarboxamide (0.053 g, 18%). MS found for $C_{25}H_{19}BrFN_5O_4S$ $(M+H)^+$: 584, 586.

Examples 194-195

N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)5-fluorophenylcarboxamide.



Example 194



Example 195

Step 1: A mixture of N-(5-bromo-2-pyridinyl)-(2-amino)5-fluorophenylcarboxamide (1.24 g, 4 mmol, 1.0 equiv), 4-cyano benzoyl chloride (0.792 g, equiv), and pyridine (3 mL) in 15 mL of dichloromethane was stirred at rt overnight. The volatile was evaporated and the residue was redissolved into EtOAc, washed with 1N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated to give N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)5-fluorophenylcarboxamide (1.14 g, 65%). MS found for $C_{20}H_{12}BrFN_4O_2$ $(M+H)^+$: 439, 441.

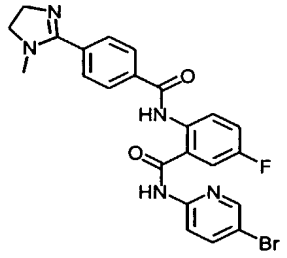
Step 2: A mixture of N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)5-fluorophenylcarboxamide (1.12 g, 2.56 mmol, 1.0 equiv), hydroxylamine-HCl (0.213 g, 1.2 equiv), and triethylamine (1 mL) in 15 mL of ethyl alcohol was stirred at 50°C

overnight. The volatile was evaporated and the residue was redissolved into EtOAc, washed with 1N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated to give N-(5-bromo-2-pyridinyl)-(2-(4-hydroxyamidinophenylcarbonyl)amino)5-fluorophenylcarboxamide (compound Example 194) (0.84 g, 70%). One third of this material was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to yield 0.20 grams (71%). MS found for $C_{20}H_{15}BrFN_5O_3$ $(M+H)^+$: 472, 474.

Step 3: A mixture of N-(5-bromo-2-pyridinyl)-(2-(4-hydroxyamidinophenylcarbonyl)amino)5-fluorophenylcarboxamide (0.56 g, 1.19 mmol, 1.0 equiv) and zinc dust (0.39 g, 5.0 equiv), in 10 mL of acetic acid was stirred at rt for 45 min. The volatile was filtered and evaporated. The residue was purified by HPLC (C18 reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN give N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)5-fluorophenyl-carboxamide (compound Example 195) (0.24 g, 44%).
MS found for $C_{20}H_{15}BrFN_5O_2$ $(M+H)^+$: 456, 458.

Example 196

N-(5-bromo-2-pyridinyl)-(2-(4-(1-methyl-2-imadazolin-2-yl)phenylcarbonyl)amino)5-fluorophenylcarboxamide.

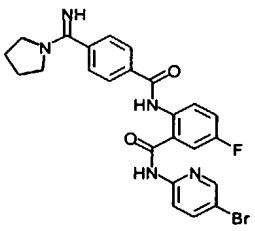


Step 1: A stream of HCl(g) was bubbled through a 0^0C solution of N-(5-bromo-2-pyridinyl)-(2-(4-cyanophenylcarbonyl)amino)5-fluorophenylcarboxamide (1.0 g, 2.3 mmol) in 30 mL of methanol until saturation. The mixture was stirred at rt overnight and evaporated. One-fifth of the resulting residue was treated with (2-aminoethyl)methylamine (0.10 g) in 10 ml methanol at rt overnight. The solvent was removed at reduced pressure and the crude product was purified by HPLC (C18

reversed phase) eluting with 0.5% TFA in H_2O/CH_3CN to give N-(5-bromo-2-pyridinyl)-(2-(4-(1-methyl-2-imadazolin-2-yl)phenylcarbonyl)amino)5-fluorophenylcarboxamide (0.082 g, 37%). MS found for $C_{23}H_{19}BrFN_5O_2$ $(M+H)^+$: 496, 498.

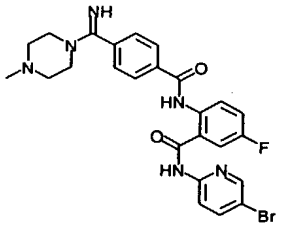
Examples 197-267

The following compounds were prepared generally according to the procedure described in Example 196.



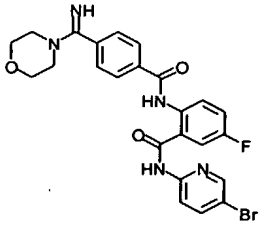
MS (M+H): 510, 512

Example 197



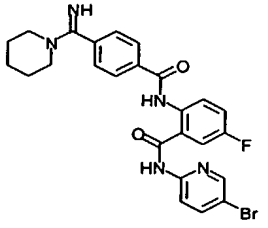
MS (M+H): 539, 541

Example 198



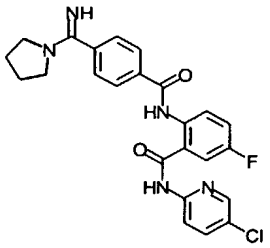
MS (M+H): 526, 528

Example 199



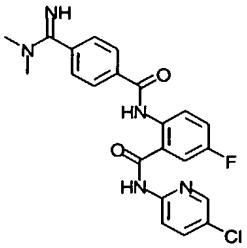
MS (M+H): 524, 526

Example 200



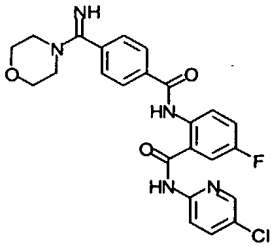
MS (M+H): 466, 468

Example 201



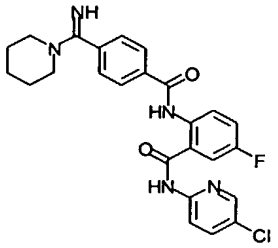
MS (M+H): 440, 442

Example 202



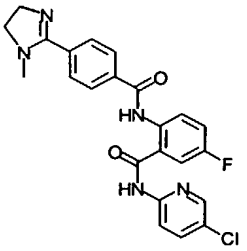
MS (M+H): 482, 484

Example 203



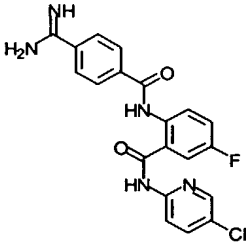
MS (M+H): 480, 482

Example 204



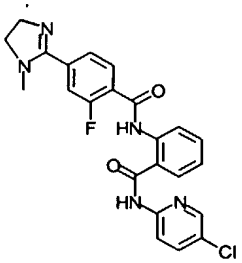
MS (M+H): 452, 454

Example 205



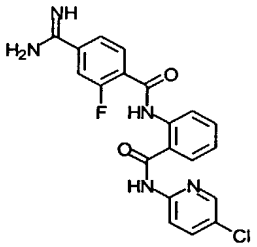
MS (M+H): 412, 414

Example 206



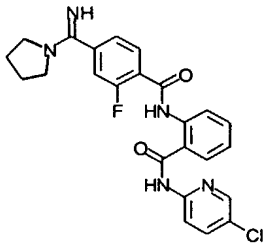
MS (M+H): 452, 454

Example 207



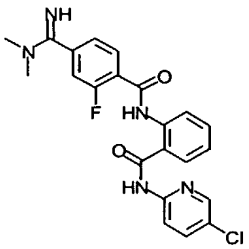
MS (M+H): 412, 414

Example 208



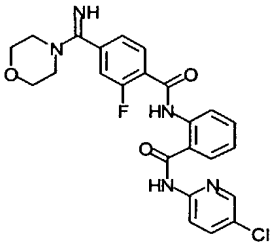
MS (M+H): 466, 468

Example 209



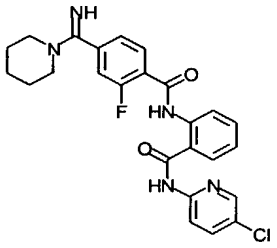
MS (M+H): 440, 442

Example 210



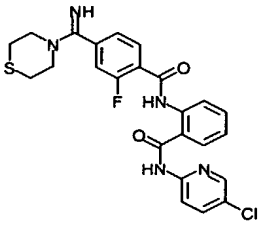
MS (M+H): 482, 484

Example 211



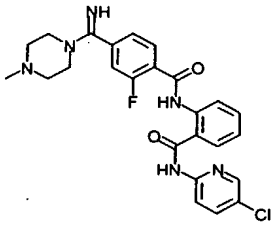
MS (M+H): 480, 482

Example 212



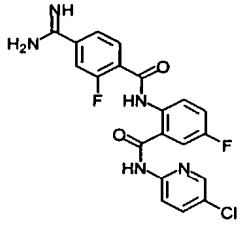
MS (M+H): 498, 500

Example 213



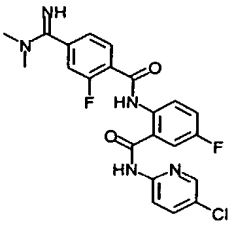
MS (M+H): 495, 497

Example 214



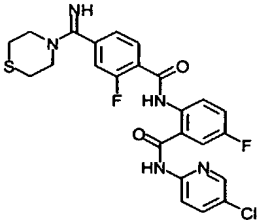
MS (M+H): 430, 432

Example 215



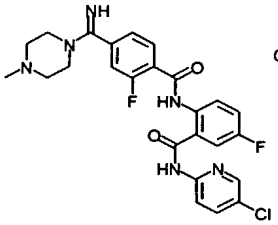
MS (M+H): 458, 460

Example 216



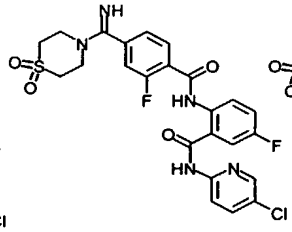
MS (M+H): 516, 518

Example 217



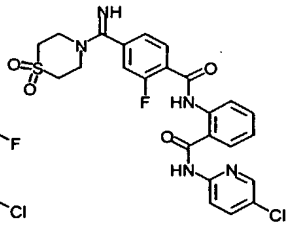
MS (M+H): 513, 515

Example 218



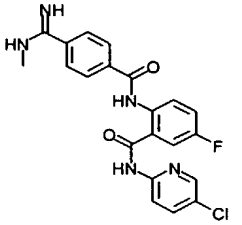
MS (M+H): 548, 550

Example 219



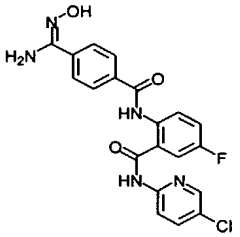
MS (M+H): 530, 532

Example 220



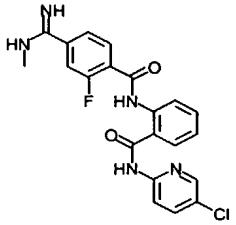
MS (M+H): 426, 428

Example 221



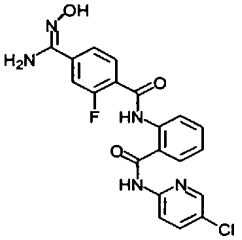
MS (M+H): 428, 430

Example 222



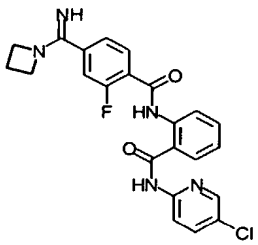
MS (M+H): 426, 428

Example 223



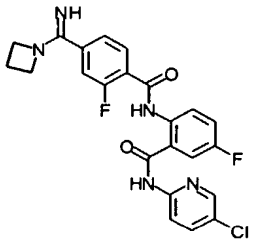
MS (M+H): 428, 430

Example 224



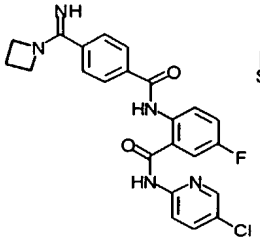
MS (M+H): 452, 454

Example 225



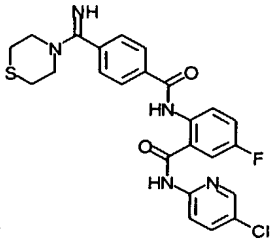
MS (M+H): 470, 472

Example 226



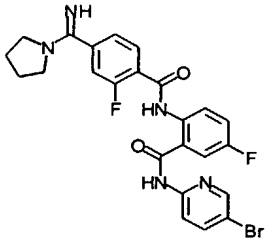
MS (M+H): 452, 454

Example 227



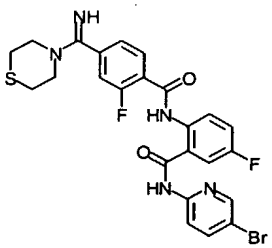
MS (M+H): 498, 500

Example 228



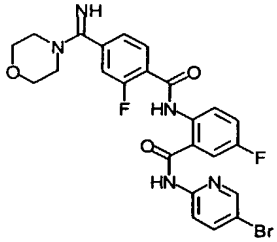
MS (M+H): 528, 530

Example 229



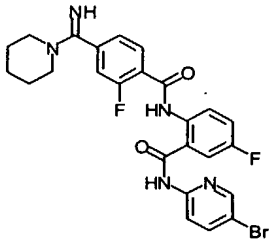
MS (M+H): 560, 562

Example 230



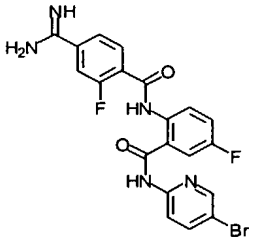
MS (M+H): 544, 546

Example 231



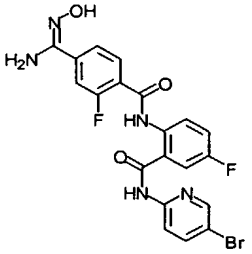
MS (M+H): 542, 544

Example 232



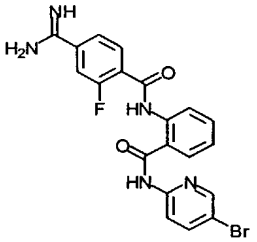
MS (M+H): 474, 476

Example 233



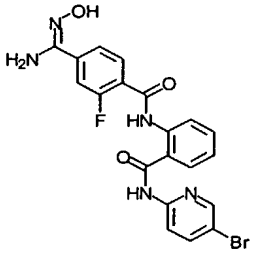
MS (M+H): 490, 492

Example 234



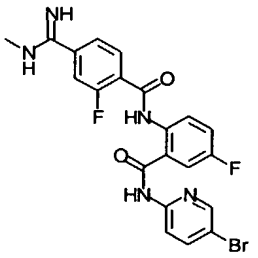
MS (M+H): 456, 458

Example 235



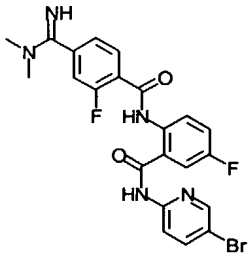
MS (M+H): 472, 474

Example 236



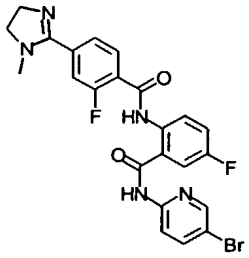
MS (M+H): 488, 490

Example 237



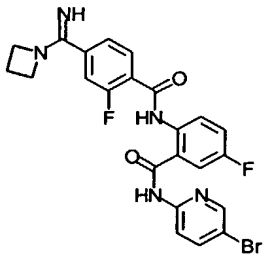
MS (M+H): 502, 504

Example 238



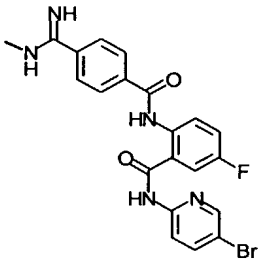
MS (M+H): 514, 516

Example 239



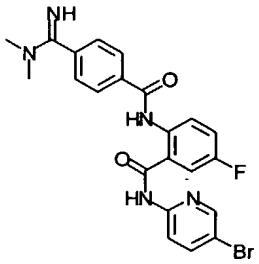
MS (M+H): 514, 516

Example 240



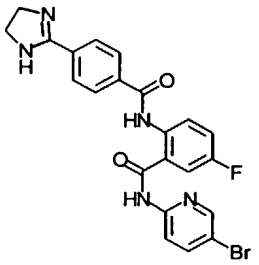
MS (M+H): 470, 472

Example 241



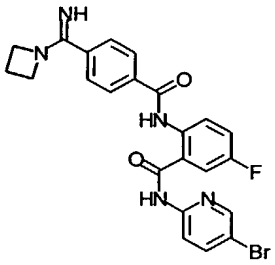
MS (M+H): 484, 486

Example 242



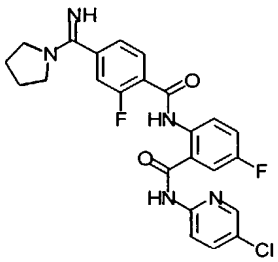
MS (M+H): 482, 484

Example 243



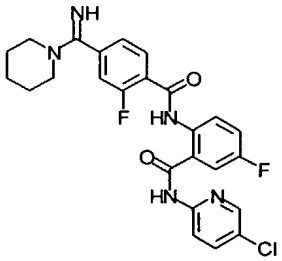
MS (M+H): 496, 498

Example 244



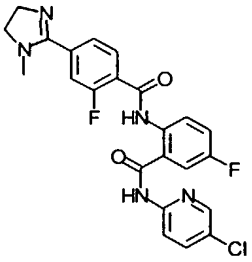
MS (M+H): 484, 486

Example 245



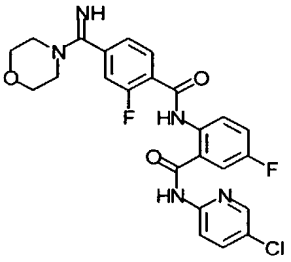
MS (M+H): 498, 500

Example 246



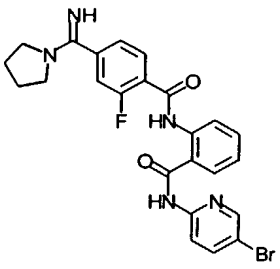
MS (M+H): 470, 472

Example 247



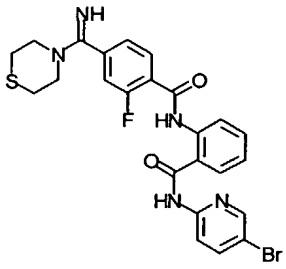
MS (M+H): 500, 502

Example 248



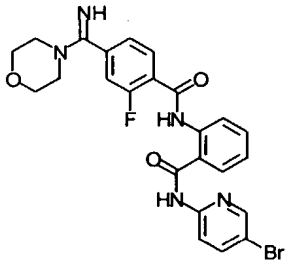
MS (M+H): 510, 512

Example 249



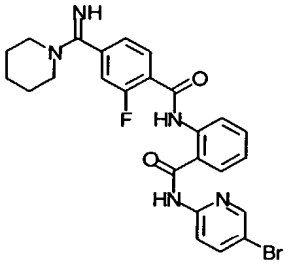
MS (M+H): 542, 544

Example 250



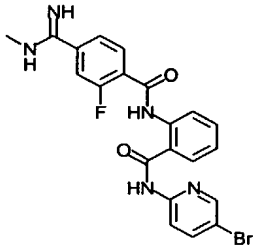
MS (M+H): 526, 528

Example 251



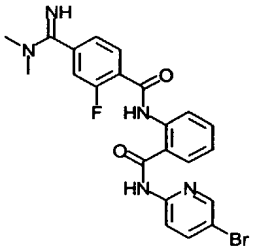
MS (M+H): 524, 526

Example 252



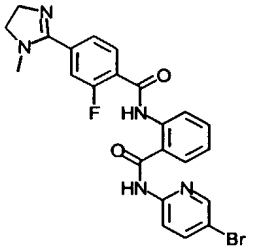
MS (M+H): 470, 472

Example 253



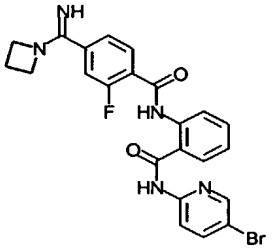
MS (M+H): 484, 486

Example 254



MS (M+H): 496, 498

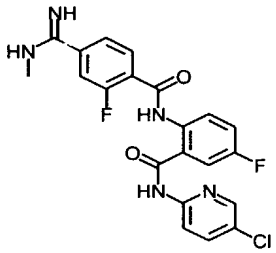
Example 255



MS (M+H): 496, 498

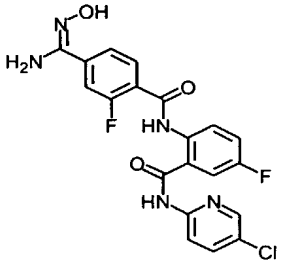
Example 256

5



MS (M+H): 444, 446

Example 257

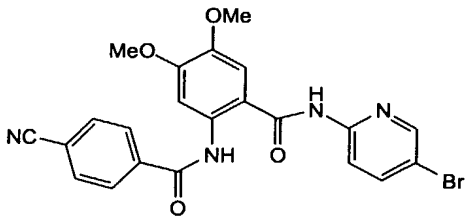


MS (M+H): 446, 448

Example 258

Example 259

N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}(4-cyanophenyl)carboxamide



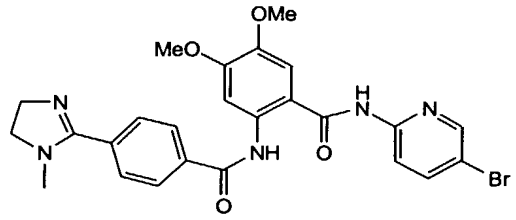
To a solution of 4,5-dimethoxy-2-nitrobenzoic acid (2.2gm, 10mmol) and 2-amino-5-bromopyridine (2.4gm, 14mmol) in anhydrous pyridine (50mL) at 0°C was added $POCl_3$ (1.9mL, 20mmol). After stirring at room temperature for 30min, the reaction was complete. The mixture was concentrated and diluted with EtOAc (200mL). The organic solution was washed with brine, dried and evaporated to give intermediate compound **1** (3.0gm, 80%). MS found for $C_{14}H_{12}BrN_3O_5$ $(M+H)^+$: 382.00, 383.95.

A mixture of intermediate compound **1** (320mg, 0.83mmol) and $SnCl_2 \cdot 2H_2O$ (900mg, 4.0mmol) in EtOAc (10mL) was refluxed for 1 hour. Reduction completed. The solid was filtered through a celite bed. The filtrate was diluted with EtOAc (50mL), and the red solution was washed with 1N aq. NaOH solution (x3) and brine, dried and evaporated to give intermediate compound **2** (230mg, 78%). MS found for $C_{14}H_{14}BrN_3O_3$ $(M+H)^+$: 352.00, 354.05.

To a solution of intermediate compound **2** (200mg, 0.57mmol) in a mixture of pyridine (3mL) and DCM (10mL) was added 4-cyanobenzoyl chloride (140mg, 0.85mmol). Precipitate formed immediately and the reaction was complete. The solid was collected by filtration and washed with DCM. After drying in vacco, the titled compound was obtained as a yellow solid in 70% yield (190mg). MS found for $C_{22}H_{17}BrN_4O_4$ $(M+H)^+$: 481.00, 483.00.

Example 260

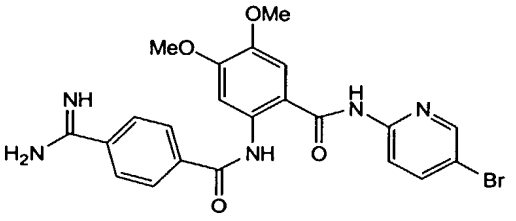
(4,5-dimethoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino}phenyl)-N-(5-bromo(2-pyridyl))carboxamide



To a solution of compound obtained in Example 259 (100mg, 0.20mmol) in 10% Et_3N/pyridine (10mL) at 0°C was bubbled dry H_2S gas to saturation. The mixture was stirred at ambient temperatures overnight, and the conversion was complete. The solvent was removed to dryness, and the residue was suspended in anhydrous acetone (10mL), followed by addition of MeI (1mL). The reaction mixture was refluxed for 1 hour. The solvent was removed by rotary evaporation. To the residue was added anhydrous MeOH (10mL) and N-methylethylenediamine (1mL). The resulting mixture was refluxed for 1 hour, concentrated and subjected to RP-HPLC purification to give the title compound. MS found for $C_{25}H_{24}BrN_5O_4$ $(M+H)^+$: 538.1, 540.1.

Example 261

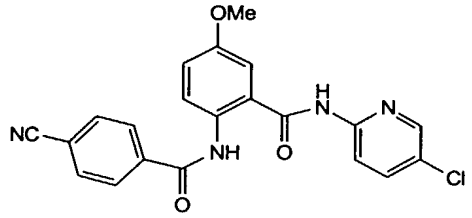
4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}carbamoyl)-benzenecarboxamidine



The title compound was obtained from the Example 259 compound according to the procedure described in Example 2. MS found for $C_{22}H_{20}BrN_5O_4$ $(M+H)^+$: 498.1, 500.0.

Example 262

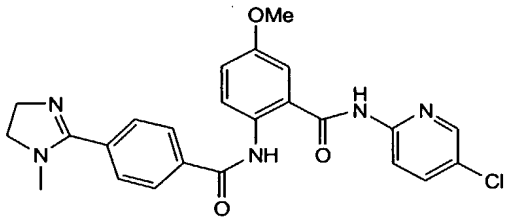
N-(5-chloro(2-pyridyl))\{2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl\}-carboxamide



This compound was obtained from 5-methoxy-2-nitrobenzoic acid and 2-amino-5-chloro-pyridine according to the procedure described in Example 259. MS found for $C_{21}H_{15}ClN_4O_3$ $(M+H)^+$: 407.0.

Example 263

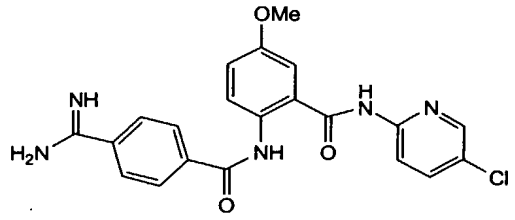
N-(5-chloro(2-pyridyl))(5-methoxy-2-\{[4-(1-methyl(2-imidazolin-2-yl))phenyl]-carbonylamino\}phenyl)carboxamide



To the suspension of the compound Example 262 (100mg) in a mixture of anhydrous MeOH (5mL) and EtOAc (5mL) at 0°C was bubbled anhydrous HCl gas to saturation. The mixture was stirred at ambient temperatures overnight. The conversion completed. The solvent was evaporated to dryness. The residue was dissolved in anhydrous MeOH (10mL), followed by addition of N-methylethylenediamine (1mL). The resulting mixture was refluxed for 1 hour, concentrated and subjected to RP-HPLC purification to give the title compound 263. MS found for $C_{24}H_{22}ClN_5O_3$ $(M+H)^+$: 464.

Example 264

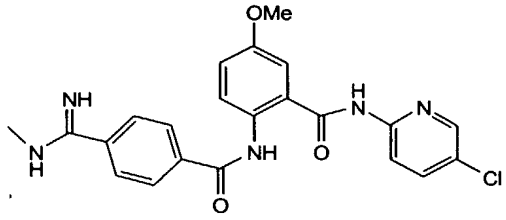
4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methoxyphenyl}carbamoyl)benzene-carboxamidine



The title compound was obtained from the Example 262 compound by procedures according to Example 262. MS found for $C_{21}H_{18}ClN_5O_3$ $(M+H)^+$: 424.

Example 265

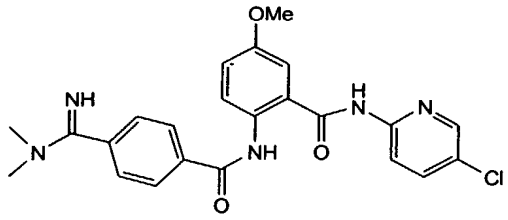
N-(5-chloro(2-pyridyl))[2-({4-[imino(methylamino)methyl]phenyl}carbonylamino)-5-methoxyphenyl]carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and methylamine according to the procedure described in Example 262. MS found for $C_{22}H_{20}ClN_5O_3$ $(M+H)^+$: 438.

Example 266

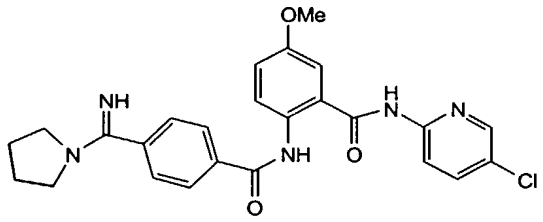
[2-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-5-methoxyphenyl]-N-(5-chloro(2-pyridyl))carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and dimethylamine according to the procedure described in example 263. MS found for $C_{23}H_{22}ClN_5O_3$ $(M+H)^+$: 452.

Example 267

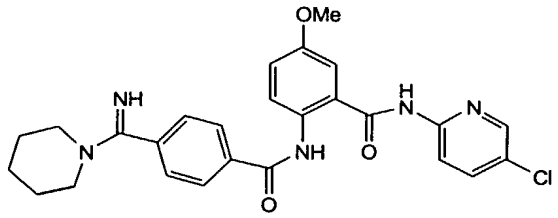
N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and pyrrolidine according to the procedure described in Example 263. MS found for $C_{25}H_{24}ClN_5O_3$ $(M+H)^+$: 478.

Example 268

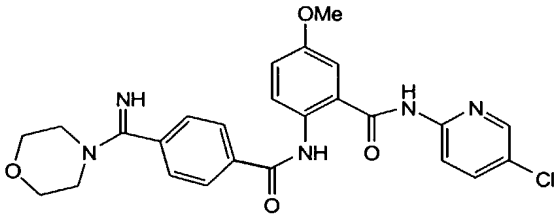
N-(5-chloro(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and piperidine according to the procedure described in Example 263. MS found for $C_{26}H_{26}ClN_5O_3$ $(M+H)^+$: 492.

Example 269

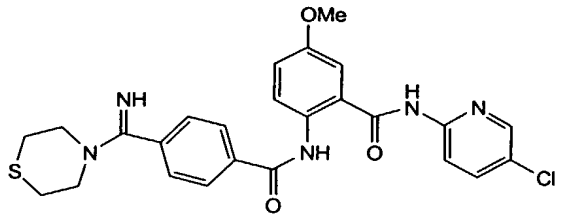
N-(5-chloro(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamin}-5-methoxyphenyl)carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and morpholine according to the procedure described in Example 263. MS found for $C_{25}H_{24}ClN_5O_4$ $(M+H)^+$: 494.1.

Example 270

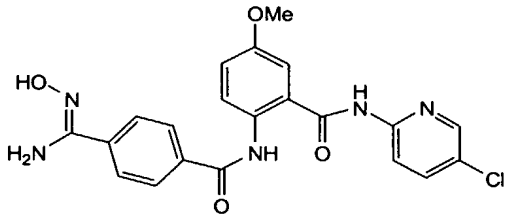
N-(5-chloro(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained from N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide and thiomorpholine according to the procedure described in Example 263. MS found for $C_{25}H_{24}ClN_5O_3S$ $(M+H)^+$: 510.

Example 271

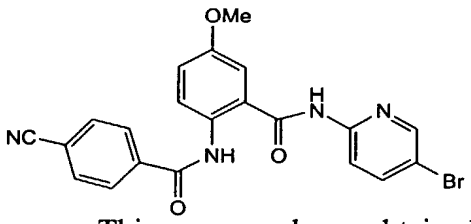
(2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide



To a suspension of compound N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide (150mg) in EtOH (10mL) was added hydroxyamine hydrochloride (80mg) and Et_3N (200μL). The mixture was stirred at 60°C overnight and the reaction was complete. The solvent was evaporated and the crude material was purified by RP-HPLC to give the title compound. MS found for $C_{21}H_{18}ClN_5O_4$ $(M+H)^+$: 440.1.

Example 272

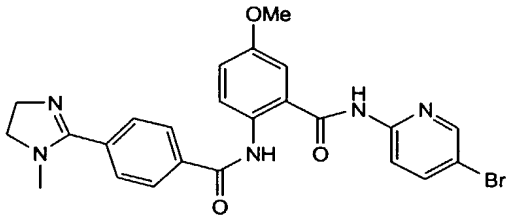
N-(5-bromo(2-pyridyl))\{2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl\}carboxamide



This compound was obtained from 5-methoxy-2-nitrobenzoic acid and 2-amino-5-bromo-pyridine according to the procedure described in Example 259. MS found for $C_{21}H_{15}BrN_4O_3$ $(M+H)^+$: 451.00, 453.00.

Example 273

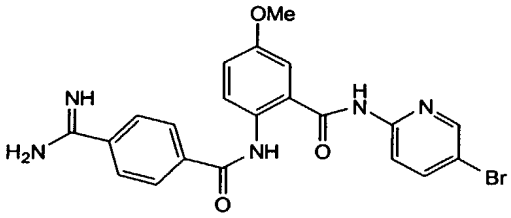
N-(5-bromo(2-pyridyl))(5-methoxy-2-\{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino\}phenyl)carboxamide



The title compound was obtained according to the procedure described Example 263. MS found for $C_{24}H_{22}BrN_5O_3$ $(M+H)^+$: 508, 510.

Example 274

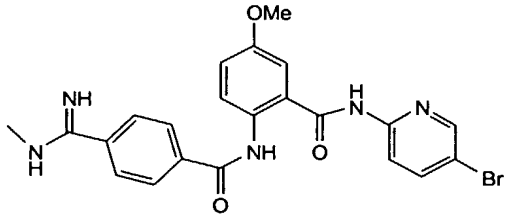
4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4-methoxyphenyl}carbamoyl)benzenecarboxamidine



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{21}H_{18}BrN_5O_3$ $(M+H)^+$: 468.05, 470.00.

Example 275

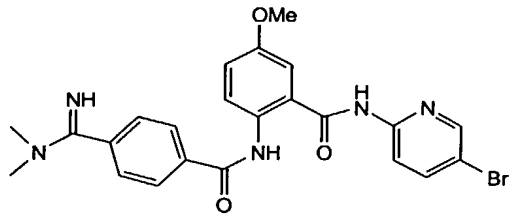
N-(5-bromo(2-pyridyl))[2-({4-[imino(methylamino)methyl]phenyl}carbonylamino)-5-methoxyphenyl]carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{22}H_{20}BrN_5O_3$ $(M+H)^+$: 482, 484.

Example 276

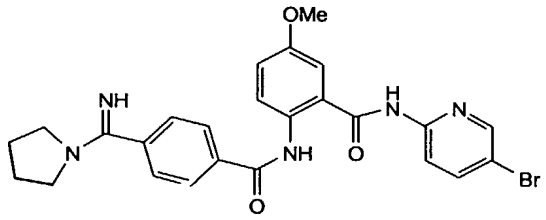
[2-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-5-methoxyphenyl]-N-(5-bromo(2-pyridyl))carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{23}H_{22}BrN_5O_3$ $(M+H)^+$: 496.1, 498.1.

Example 277

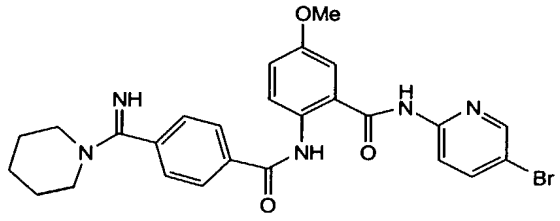
N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{25}H_{24}BrN_5O_3$ $(M+H)^+$: 522, 524.

Example 278

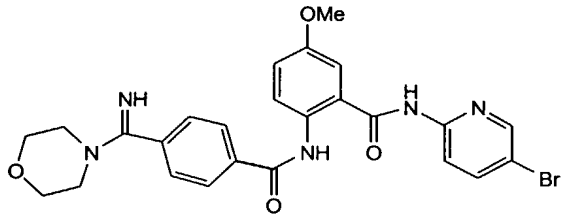
N-(N-(5-bromo(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{26}H_{26}BrN_5O_3$ $(M+H)^+$: 536.1, 538.1.

Example 279

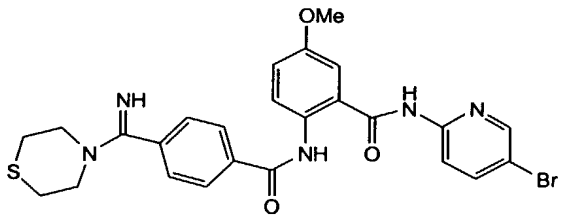
N-(5-bromo(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{25}H_{24}BrN_5O_4$ $(M+H)^+$: 538.1, 540.1.

Example 280

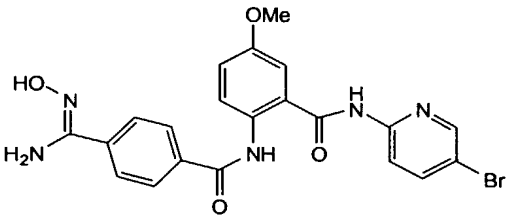
N-(5-bromo(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide



The title compound was obtained according to the procedure described in Example 263. MS found for $C_{25}H_{24}BrN_5O_3S$ $(M+H)^+$: 554.1, 556.05.

Example 281

(2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-bromo(2-pyridyl))carboxamide



The title compound was obtained according to the procedure described in Example 270. MS found for $C_{21}H_{18}BrN_5O_4$ $(M+H)^+$: 484.1, 486.0.